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Milk Intake in Early and Late Adulthood and Risk of Osteoporotic Hip Fractures in Utah

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MILK INTAKE IN EARLY AND LATE ADULTHOOD AND RISK OF OSTEOPOROTIC HIP FRACTURES IN UTAH

by

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ABSTRACT

Milk Intake in Early and Late Adulthood and Risk of

Osteoporotic Hip Fractures in Utah

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The relationship between milk intake and risk of osteoporotic fractures is uncertain. Associations between milk intake and milk avoidance in relation to osteoporotic hip fracture were examined in the Utah Study of Nutrition and Bone Health (USNBH), a statewide case-control study. Cases were ascertained at Utah hospitals treating 98 percent of hip fractures during 1997-2001 and included 1188 men and women aged 50-89 years. Age- and gender-matched controls were randomly selected from Utah driver's license and Medicare databases (N= 1324). In-person interviews were conducted and participants reported frequency of milk intake per week at age 18 and during pregnancy among women who reported being pregnant. Milk avoidance for a period of more than one year and duration of milk avoidance were also reported. Diet and supplement intake in the one-year period before fracture (cases) or the interview (controls) was assessed using a picture-sort food frequency questionnaire. Milk

consumption frequency was categorized into four levels of intake at each life stage. Total calcium intake was categorized into quintiles of distribution of intake. Logistic regression models were used to examine associations between milk intake and milk avoidance and risk of hip fracture while controlling for the potential confounding effects of gender, age, body mass index, alcohol use, smoking, physical activity, estrogen use, and total calorie, protein, calcium, and vitamin D intake. Recent milk intake, milk intake during pregnancy, and milk avoidance duration were not associated with risk of hip fracture. A borderline association was found at age 18 showing a decreased risk of hip fracture among those in the highest quartile ($\geq$ 15 cups of milk per week) of milk intake (odds ratio (OR): 0.86, 95 percent confidence interval (CI): 0.75, 1.00; P = 0.046). Milk avoidance for a year or more was associated with an increased risk of hip fracture compared to those who did not avoid milk (OR: 1.38, 95 percent CI: 1.07, 1.78). A significant interaction was found between milk avoidance and quintile of total calcium intake (P = 0.02). Milk avoidance was associated with a significantly higher risk of hip fracture at the lowest two quintiles of calcium intake (OR: 1.72, 95 percent CI: 1.26, 2.17; P = 0.02 and OR: 1.58, 95 percent CI: 1.01, 2.15; P = 0.01, respectively) but was not associated with elevated risk among those with higher calcium intakes. In conclusion, milk intake during pregnancy for women, and in the year before hip fracture (for cases) or before interview (for controls), was not associated with hip fracture risk. The highest level of milk intake at age 18 was associated with decreased risk of hip fracture. Avoidance of milk for one year or more was associated with hip fracture risk, but only among those with low calcium intake (Q1 and Q2).

(179 pages)

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CHAPTER I

INTRODUCTION AND BACKGROUND

Abstract

Hip fracture is the most detrimental of osteoporotic fractures for the individual, the most expensive for healthcare and has become an increasingly significant public health concern. Because of the multiple issues of hip fracture it is important to consider ways to prevent the devastating disease, osteoporosis. Diet is a modifiable element in bone health and nutrition must be considered. Although several studies have been conducted on specific nutrients and supplementation, very few studies have been carried out to consider whole foods, such as milk, in relation to hip fracture. Nutritional improvement may result by increasing milk in the diet and in turn, decreasing the risk of osteoporosis and hip fracture. Data from The Utah Study of Nutrition and Bone Health will be evaluated to determine whether an association exists between milk intake and hip fracture. Background, hypotheses, methods and statistical procedures are included.

Introduction

The aging adult faces many physiological changes and health challenges. The problems associated with aging greatly contribute to the cost of health care and significantly reduce quality of life. Osteoporotic fractures, particularly hip fracture, are public health concerns in relation to aging (1).

Hip fractures are found more commonly in individuals with numerous dietary deficiencies. Because diet is a modifiable factor and can lead to prevention of

osteoporosis, nutritional issues in relation to hip fracture are of interest. Numerous studies have provided information on calcium and vitamin D intake but very few studies have been conducted to consider whole foods for calcium intake such as milk and other dairy products (2). Interestingly, research investigating dietary patterns in association with decreased calcium intake found that diets low in calcium were also deficient in other nutrients such as protein and phosphorus (3). Nutritional improvement may result by increasing milk in the diet and in so doing, decreasing the risk of osteoporosis and hip fracture (2, 4).

The Utah Study of Nutrition and Bone Health (USNBH) is a case-control study including dietary data that can be used to examine the relationship between milk intake throughout life and risk of hip fracture later in life. The effect of milk avoidance at any time during the life cycle can also be evaluated.

Background

Osteoporotic hip fracture affects around 250,000 persons in the United States per year and these numbers are increasing (1). Of those that suffer from hip fracture there is a 12-20% reduction in survival and many will never regain their regular pre-fracture activities of daily living (5). Consideration of ways to prevent loss of bone mass and the destructive disease, osteoporosis is of great importance.

Bone mass is dependent upon a number of factors including genes, hormones, ethnicity, gender, exercise, body weight, disease, medical treatments and nutrition (6, 7). These factors contribute to bone loss and osteoporosis through influencing bone mass accumulation during growth and bone mass maintenance during aging. Many of these

factors cannot be avoided and because osteoporosis is a multi-factorial disease we can assume that no single intervention, whether medicinal, hormonal or nutritional, can completely prevent osteoporotic hip fracture (6).

Milk is a complex food that contains calcium as well as other important nutrients needed for bone health including protein, phosphorus, magnesium, zinc, riboflavin, thiamin, vitamin B12 and energy (2-4, 8). It contains more of the above listed nutrients per unit energy than other common foods in the adult diet (6). Because milk is more commonly consumed than other dairy foods in most Western diets (9) and its nutritional content is well established, it can be considered a good nutrient vehicle to study in association with bone health. Milk is also heavily marketed as beneficial for bone health and is of interest since research has not exclusively shown this result (6, 10, 11).

The amount of milk consumed during particular stages of life may prove more beneficial than another stage. One study has shown that increased milk intake does not positively effect fracture risk in women over fifty years of age, but that there may be a benefit in women under thirty years of age (12). Higher milk consumption during adulthood was found significantly and independently associated with higher bone mineral density in the hip more than milk intake during adolescence (13). The role of milk intake in risk of osteoporotic fracture is inconclusive.

Primary prevention of osteoporosis and hip fracture may be achieved by accumulating the largest peak bone mass (PBM) possible within the limitations of the genetic possibilities (14, 15). Since bone is composed of protein and mineral, nutritional factors can influence bone mass and help fulfill the genetic potential of skeletal strength. Nutritional deficiencies restrict bone growth and limit achievable PBM of an individual

(6, 14). Nutritional factors affecting bone health include energy, protein, vitamins such as vitamin D, and minerals such as calcium, zinc, magnesium and phosphorus (14, 16). PBM occurs from ages as early as 14 or 15 years in females and 17-18 years in males to as late as 35 years in either sex (14, 17, 18). By evaluating milk intake at age 18, a time when PBM of the hip is near its peak (19), an association between milk intake and risk of hip fracture may be detected.

During pregnancy a significant transfer of calcium occurs from the mother to the fetus, thus decreasing the bone mass of the mother. This theoretically places the mother at an increased risk of osteoporosis and hip fracture later in life, especially if there were no efforts to maintain positive calcium balance during pregnancy (20). Calcium lost during pregnancy may be replaced by consuming high levels of calcium through milk, other foods, and supplements (21, 22). Pregnancy has not been found significant in association to risk of hip fracture and little information is available on this topic (20, 23-25). Also, few studies have been done to show whether an increase of milk consumption during pregnancy would have a protective effect in the incidence of hip fracture later in life.

Osteoporosis most often presents after age 50 and a dramatic rise in the incidence of hip fracture occurs after age 65 years (26). White women over 50 years have a 16% lifetime chance of suffering from a hip fracture and white men have a 5% lifetime risk (27). Because of the occurrence late in life, consideration and prevention of osteoporosis is often postponed. Nutritional benefits of drinking milk at an older age are still attainable and may decrease fracture risk (2, 13, 28). Milk consumption decreases with

age (13). Reasons for this decrease is unknown but suspected to be secondary to health problems and because total food intake also decreases as people age (4, 13).

Bone is a dynamic organ. Bone mass is determined by the balance of formation and resorption during bone remodeling (17). In this process small amounts of old bone are resorbed and replaced by new bone formation. If the resorption of old bone surpasses formation, an individuals bone mass will decline. If the formation of the new bone surpasses the breakdown, bone mass will increase. Heaney et al. showed that increased milk consumption by men and women, aged 55 to 85 years, significantly decreased bone resorption by about 13 percent (2). This is important because decreased bone resorption may be the first step in maintaining bone density and decrease risk of hip fracture.

The evidence relating decreased hip fracture risk to increased milk intake is unclear and contradictory. An actual increased risk of hip fracture was found in association with increased milk and dairy products (29, 30). Other studies have not shown any relation between milk consumption over age 50 and hip fracture, whether protective or detrimental (31-33). An extensive review of the literature on milk intake and osteoporosis follows including analyses of data on milk consumption and hip fracture risk in Utah.

Milk avoidance may be detrimental to some persons. Children who avoid milk have shorter stature, smaller skeletons, lower total body bone mineral content and lower bone mineral density at the femoral neck and hip trochanter (34). These children, because of their lack of essential nutrients needed for bone growth, also experienced a greater number of fractures (34, 35). Reasons for milk avoidance are lactose intolerance, taste dislike, the availability of competitive beverages such as soda, concern about body

weight, and family or personal lifestyle choice (34, 36). Postmenopausal women with low milk consumption throughout life, due to lactose intolerance and malabsorption, had an increased risk of developing osteoporosis (12). This same evidence suggests that milk avoidance throughout the life cycle may cause detrimental effects on the bone and be a predictor of osteoporosis and hip fracture later in life, yet the vast majority of adults in the world are lactose intolerant and do not drink milk (37).

Hypotheses

The following hypotheses will be examined in the Utah population sample aged 50 to 89 years:

- Milk intake at age 18 is associated with risk of hip fracture; persons with greater milk intake at this time will have a lower risk of hip fracture compared to those with low milk intake.
- Among women that reported being pregnant, milk intake during pregnancy is associated with risk of hip fracture; women with greater milk intake at this time will have a lower risk of hip fracture compared to those with low milk intake.
- Milk intake in men and women aged 50-89 years is associated with risk of hip fracture; persons with greater milk intake at this time will have a lower risk of hip fracture compared to those with low milk intake.
- Milk avoidance at any time during life is associated with risk of hip fracture; as the number of years of milk avoidance increase, risk of hip fracture will also increase.

- The associations between milk intake and risk of hip fracture is independent of other factors known to be associated with hip fracture, including age, gender, height, estrogen use, physical activity, vitamin D intake, protein intake and calcium supplementation.

Methods

The USNBH is a statewide case-control study with data on risk factors for hip fracture in the elderly population ages 50 to 89 years. The data were obtained during 1997 - 2001. Information collected during the direct interviews was based on recall from each participant including the amount of milk intake per week at age eighteen years and during pregnancy for women who reported being pregnant. Dietary intake during the past year for controls and during the one-year period before hip fracture for cases was assessed via a food frequency questionnaire (FFQ) (38). Milk was one of the food items reported. Participants were also asked to recall if they avoided milk for a year or more. If so, the duration of milk avoidance was reported. The USNBH data was used to determine if milk intake has important public health implications related to osteoporotic hip fracture.

Logistic regressions models were used to examine the relationships between milk consumption variables and risk of hip fracture. Odds ratios were calculated using the lowest consumption or nutrient quartile as the reference intake. Milk avoidance was considered a binomial variable and included those who avoided milk for a year or more and those who did not avoid milk. Multivariate models were adjusted for the effects of potential confounders including age, gender, body mass index, vitamin D intake, calcium

supplementation, total calorie intake, protein intake, smoking history, estrogen replacement therapy, physical activity and/or alcohol consumption.

Results from this analysis may provide direction for the dietary instruction offered to teenagers, pregnant women and aging adults regarding milk consumption and bone health. Results will also provide more information on consequences of milk avoidance in relation to osteoporotic hip fracture.

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CHAPTER II

MILK INTAKE AND RISK OF OSTEOPOROTIC HIP FRACTURE: A REVIEW

Abstract

The role of milk in osteoporotic hip fracture is uncertain. Clarification of the association between milk intake and risk of hip fracture is needed to provide appropriate recommendations for nutrition in bone health. Milk is heavily marketed as beneficial for bone and more commonly consumed than other dairy products in the United States. Milk provides several key nutrients related to bone such as calcium, phosphorus, protein, and energy. Adequate milk consumption during specific stages in life may help decrease bone loss and its most serious outcome--hip fracture. Alternately, milk, which most adults in the world cannot tolerate or do not drink, may not be an important factor in relation to hip fracture. Specific life periods have been reviewed including time of peak bone mass, pregnancy, and older adulthood. Avoidance of milk at any stage of life, from childhood to geriatric, for any reason, whether it be personal choice or disease related, has also been reviewed. Understanding the benefits of milk intake, if any, at each stage in life and its associated impact on hip fracture may aid dietary community outreach education and public awareness about current milk consumption recommendations.

Introduction

Prevention of bone loss through diet is complex and involves several nutrients such as calcium, vitamin D, protein, phosphorous, vitamins B12 and B6, potassium,

magnesium, zinc, riboflavin, thiamin, and energy (1-7). Most research has focused on calcium and vitamin D, and new studies are finding evidence of other involved nutritional factors (7). A low intake of calcium is considered to be a risk factor for osteoporotic fractures; including hip fracture. Diets low in calcium are also deficient in many other nutrients such as protein, phosphorus, and energy (2, 8). Hip fractures are most commonly found in individuals with numerous levels of dietary deficiencies (8). Undernutrition is considered a risk factor for hip fracture because it can cause an increased susceptibility to fall by impairing coordination and decreasing muscle strength (9). Undernutrition can also increase risk of hip fracture because of associated low bone mass (10) and because of the reduction in the protective layer of soft tissue padding around an osteoporotic hip (9).

Milk is a complex beverage that contains calcium and other nutrients needed for bone health. It contains more sources of calcium, phosphorus, magnesium, potassium, zinc, and protein per unit of energy than other characteristic foods in the adult diet (8). Because milk is consumed more often than other dairy in most Western diets (11), and its nutritional content is well understood, it can be considered a good nutrient vehicle to study in association with bone health. Milk is also strongly marketed as valuable for the skeleton and is of interest since research is not conclusive (8, 12, 13).

Milk can be an important food for the development of the body and all living tissue, including bone. Although the essential nutrients found in milk may work to sustain bone growth and maintenance, and lead to dietary prevention of hip fracture (8), most adults worldwide cannot tolerate this beverage or choose not to drink it for various

reasons (14-18). Furthermore, the research has shown unconvincing results on the role of milk in relation to hip fracture.

Background

Osteoporosis is a devastating disease affecting elderly persons throughout the world (19). The World Health Organization defines this disease as a "systematic skeletal disease characterized by low bone mass and micro-architectural alterations associated with increased fragility and susceptibility to fracture" (20). A decrease in bone mass is the most directly measurable aspect of osteoporosis and has been proven a risk factor for fracture (21), and is usually measured and assessed using bone mineral density (BMD) as a marker (22). Heaney, an expert in the arena of bone health, has suggested that when all variables related to hip fracture are held equal, a 12% -15% loss of bone mass can cause fracture risk to double (23).

Hip fracture is the most detrimental of osteoporotic fractures and the most costly for healthcare (24, 25). Hip fractures occur in around 250,000 persons in the United States per year (24, 26, 27), and 1.6 million hip fractures worldwide in 1990 is projected to increase to 6.26 million in the year 2050 (19). The chance of experiencing a hip fracture is equivalent to the lifetime risk of developing breast, uterine and ovarian cancer in white women and developing prostate cancer in white men (27). Of those that suffer from hip fracture, there is a 12%- 20% reduction in survival and survivors may not regain their regular pre-fracture activities of daily living (28). Because of the substantial and multiple consequences related to hip fracture, it is important to consider ways to prevent loss of skeletal mass and the originating disease osteoporosis.

Bone mass is dependent upon a number of different variables, that include genes, hormones, race, gender, exercise, body weight, disease, medical treatments, and nutrition (29, 30). These factors have been known to influence bone mass accumulation during growth and bone mass maintenance during aging. These factors have also been noted to contribute to bone loss and osteoporosis (8, 27). Unfortunately, many of these variables cannot be avoided. Because osteoporosis is a multi-factorial disease, we can assume that no single intervention, whether medicinal, hormonal or nutritional, can completely answer the question of how to prevent osteoporosis and associated hip fracture (8).

The majority of hip fracture cases are seen among females and most research has been performed on women (31, 32). Gender is one of the most pronounced risk factors for hip fracture. Bone turnover and loss accelerate at the time of menopause secondary to the effects of reduced estrogen (7, 10, 22). This occurrence affects both calcium absorption and retention and places postmenopausal women at increased risk of osteoporosis (10, 22). Less attention has been directed toward males even though 20% of all hip fractures occur in men (25, 26).

Other specific factors associated with decreased bone mass and risk of hip fracture include: increased age (28), increased height (33-35), smoking (36), history of previous falls or fractures (33), medical conditions and medications (28, 33, 35, 37), low level of physical activity (33), low body mass index (33, 37), and dietary intake (8, 22, 38, 39).

Diet is a modifiable lifestyle factor that can lead to increased prevention of osteoporotic fracture, thus it is important to consider nutrition in relation to hip fracture.

Protein-energy malnutrition is the most common nutritional deficiency found in the elderly and may be a risk factor for osteoporotic fractures (9, 22). Milk is a well-defined dietary source of not only protein and energy, but also several other nutrients that may aid in the prevention of osteoporosis (1-4). The amount of milk consumed during particular stages of life, such as adolescents, pregnancy, and older adulthood, may prove more beneficial than other stages and may provide more insight on necessary recommendations for milk intake throughout the lifecycle (40-42). Although it seems plausible that milk intake might decrease the risk of hip fracture, the research is inconclusive.

The Effect of Milk on Bone Characteristics

Bone is a dynamic organ. Bone mass is determined by the balance of formation and resorption in the bone remodeling process (27, 43). During bone remodeling, small amounts of old bone are resorbed, or broken down, and then replaced by new bone. If the resorption of old bone surpasses formation, an individuals bone mass will decrease. If the formation of the new bone surpasses the breakdown, bone mass will increase. Heaney et al. has shown that increased milk consumption by men and women, aged 55 to 85 years, significantly decreased bone resorption by about 13% (1). Toba et al. found that milk whey protein (a by-product of milk during the cheese making process) suppresses resorption and enhances bone strength in ovariectomized rats (44). Another similar finding showed that milk decreased bone remodeling, more so than calcium supplements, helping to maintain bone strength (45). This is important because decreased bone resorption and remodeling may be the first step in maintaining bone density and decreasing the risk of osteoporosis and hip fracture.

Bone growth can be stunted by malnutrition and is dependant upon dietary intake to provide the materials necessary for structural and mechanical properties (22). Poor nutritional status, occurring secondary to inadequate intake, has shown a decrease in muscle mass, bone mass, and soft tissues and increases the risk of hip fracture (35, 39). Bone health must be maintained through diet even once bone growth has ceased and sufficient raw materials at all stages of life are required (21).

Increased milk consumption increases the dietary intake of several nutrients including protein, calcium, phosphorus, vitamins D, A, B-12 and B-6, potassium, magnesium, zinc, riboflavin, thiamin, and energy (1-6). Most of these nutrients have shown some kind of positive or negative association with bone health (46, 47).

Calcium, phosphorous, and protein make up nearly 95% of the bony skeleton (8). High intakes of protein and phosphorus may reduce calcium absorption and increase the related problems of calcium deficiency (8). The high protein content of milk has been observed to increase urinary calcium excretion, thus causing a possible negative effect on calcium balance and BMD (7, 8, 38, 48). But increased protein has also been shown to increase calcium absorption thus producing no change in calcium homeostasis (49, 50). Further, too little protein has shown harmful effects on bone health and increased risk of fracture in the elderly (7, 38, 39, 51). Ilich et al. and Huang et al. found, through separate studies on Caucasian postmenopausal women, that protein and energy were both independent factors showing a positive effect on BMD and hip fracture risk, respectively (39, 46). The beneficial effects of protein on bone may be dependent on other factors in the diet such as calcium and vitamin D intake (38, 46). Phosphorus may have a negative effect on calcium absorption because it may cause hyperparathyroidism, which can

increase bone resorption (48). It is also believed to form insoluble complexes with calcium, thus further decreasing possible calcium absorption (52). Although dietary phosphorus causes an increase in endogenous fecal calcium excretion (38, 52), the abilities of this same mineral can actually decrease urinary calcium excretion (38, 48, 52). Recker et al. found that the protein and phosphorous in milk did not decrease the amount of calcium absorbed or excreted any more than if calcium was coming from another source (53). A review of protein and phosphorous in relation to calcium absorption efficiency has not shown solid evidence of decreased bone mass (52), and in fact, seems necessary for bone strength (22).

Vitamin D has proven important for bone because of its ability to maintain calcium homeostasis (22) and positive effect on calcium absorption (7), especially in those who consume low levels of calcium (21). Low vitamin D status is more common among older adults because of decreased sun exposure and decreased plasma vitamin D and is associated with increased risk of hip fracture (7, 35). In the 18-year follow-up analysis of the Nurses Health Study, Feskanich et al. found a 37% lower risk of hip fracture among women consuming high levels of vitamin D from food and supplements, but no association with calcium or milk intake (54). Other studies combining vitamin D with calcium found a decreased fracture risk when compared to placebo groups (55, 56). The role of vitamin D in bone health has been clearly established secondary to its positive effect on calcium absorption (7, 22).

Vitamin A has been associated with an increased risk of hip fracture due to the stimulation of osteoclast formation and increased bone resorption (7, 57). The Nurses Health Study found that women consuming over 3000 micrograms of retinol per day

compared to 1250 micrograms were 1.5 times more likely to suffer from hip fracture (57). Michaelsson and Melhus et al. found that among Swedish women (58) and men (59), levels of vitamin A intake above 1500 micrograms per day for women and 75.6 micrograms per deciliter for men, had a relative risk of 2.1 and 2.5, respectively, for hip fracture. A 10% lower BMD was also seen among the women among the highest group of retinol intake (58). Animal and *in vitro* studies also show links between high retinol intake and increased bone resorption and decreased bone formation (60, 61). Conflicting information has shown no effect of vitamin A, although more and more evidence is becoming available supporting a negative role on bone health and fracture risk (7).

Potassium and magnesium have both been found to be significantly beneficial on BMD among men and women (7, 46, 47). About 59% of the body's magnesium is found in bone, where it may enhance bone quality by influencing hydroxyapatite crystal growth (29). Further evidence has shown dietary magnesium to negatively predict urinary excretion of bone resorption markers in postmenopausal women (22). Potassium aids in bone health through promoting renal calcium retention and maintaining positive calcium balance (7).

Zinc is a bone matrix constituent and a necessary cofactor for enzymes involved in the production of the bone matrix (7), and results have demonstrated increased BMD of the spine with higher intakes of this mineral (46, 47, 62). Zinc is also considered important because of its ability to stimulate production of insulin-like growth factor I (IGF-I), and increase bone formation (7, 22).

Vitamin B12 has been shown to increase markers of bone formation and improve BMD in patients with pernicious anemia secondary to its role in DNA synthesis (7).

Postmenopausal women with pernicious anemia have been found to have a 1.9 times greater risk of proximal femur fractures than those without this anemia (63). Replacement of vitamin B12 among those with pernicious anemia has also been found to normalize BMD compared to controls (64).

Multi-collinearity among nutrients in foods and the nutrition status of an individual may be more important in bone health and risk of hip fracture than just one particular nutrient (7, 39). Milk is composed of many beneficial nutrients for bone health, and because these nutrients are packaged together, it may be an efficient way to prevent bone loss.

Milk and Dairy Products

Dairy products contain several essential nutrients important for skeletal strength and maintenance. Heaney stated that "their effects on bone health are likely more than can be accounted for by any single constituent, and indeed, the totality of their effects may be more than the sum of their parts" (8). Dairy products provide over 50% of total calcium, 19% of protein and approximately 9% of the total amount of fat in an average Western diet (65). The key nutrients found in milk, as previously mentioned, are also prevalent in other dairy products (2, 8, 23, 65, 66). Calcium in most non-dairy sources is not as concentrated, which may place a barrier to obtaining the recommended dietary allowances for calcium if dairy products are not regularly ingested (12, 67, 68). An adequate Western diet would be difficult to attain without including dairy foods (8, 12, 67, 68). Alternatively, it is possible to attain adequate calcium through ingestion of calcium-rich plant foods and calcium fortified foods or supplements (13, 68).

The role of dairy foods in relation to bone health is still uncertain. After a review of the literature, Weinsier et al. determined that the scientific evidence now available is not adequate enough to support a recommendation for dairy products in prevention of bone loss secondary to an under-representation of the research on men and ethnic groups (12). This review did find a correlation between bone health and dairy products in women under age 30, but no positive effect on bone mass or hip fracture in women over age 50 (12). Using the same evidence and publications as Weinsier et al., only categorizing the research differently, Weaver and Heaney concluded that adequate dairy consumption is supportive of good bone health at all ages (8, 23, 69). A recent review of clinical, longitudinal, retrospective and cross-sectional studies published on the relationship between dairy and calcium intake on bone mineralization or fracture risk in individuals aged 1 –25 years found no consistent benefit from either dairy products specifically or total dietary calcium intake (13). Calcium supplementation did show a modest benefit on BMD in children and adolescents (13). Contradictory reports have been found showing an actual increased risk of hip fracture in association with increased dairy consumption at ages 20 and in older aged individuals (36). Ecological research implies that populations with high calcium and protein intakes due to the ingestion of dairy products have the highest rate of hip fracture (70). Populations susceptible to osteoporosis, such as the United States, New Zealand and Sweden, tend to consume more, rather than less calcium and protein, although a specific causal agent is unknown (70). The research has not completely supported the assumption that dairy products decrease osteoporotic bone loss and fracture risk (54).

Milk vs. Other Dairy Products

Milk consumption may be more beneficial than other dairy products in relation to bone health. Milk has been shown to have a positive effect on bone mass, while total dairy food and cheese intakes have not (12, 41). Also, no significant difference among calcium absorption comparing several different dairy products and calcium carbonate supplements has been found (53). In the MEDOS Study, low milk and cheese intakes were associated with increased risk of hip fracture in men over 50, and the association with cheese was stronger than that of milk (31). Despite these studies, biologically all dairy foods cannot be considered equal vehicles of calcium secondary to their different ratios of protein, sodium, potassium and vitamin A (12). Production of cottage cheese results in a decrease of calcium and potassium content by about half that of milk and increases protein content by 4 times and sodium content by around 8 times (12). Calcium and potassium show favorable affects on skeletal mass while large amounts of sodium, protein, and vitamin A have adverse affects (7, 12)

High sodium intake may be a disadvantage to bone health due to its effect on increased urinary calcium loss (7, 71). Through measurements of urinary sodium excretion, high sodium intake is associated with an increased bone loss at the hip site (71). Similar results on urinary calcium loss are seen with high levels of protein intake (7, 48). High protein cheeses also produce a potential renal acid load of approximately 25 times that of milk (12). At low protein and sodium intake, the requirement of calcium may be as little as 400 mg/day, while if these two nutrients are elevated in the diet, calcium requirements may be as high as 2000 mg/day to maintain calcium balance (72).

Because of the higher ratio of calcium to sodium and protein compared to other dairy products, milk may have a more positive impact on bone density.

Milk may be more appropriate to study in relation to bone health than other dairy foods, not only because of its nutritional value, but because it is more commonly consumed in the United States (11) and is less expensive (40). Approximately 181 pounds of milk per capita year was consumed in the United States during 2004 compared to 24 pounds of cheese and 9 pounds of yogurt (11).

Calcium in Relation to Bone Health

Physical activity and skeletal muscle mass often decrease during the aging process (9, 23). Age-related changes decrease the mechanical loading of the skeleton, leading to weaker, more brittle bones (73). This may increase the calcium requirements of the elderly in order to provide raw material to help maintain skeletal strength (23). Other aging processes that affect the requirements of calcium in the elderly include; decreased calcium absorption efficiency secondary to a decrease in solar exposure and vitamin D synthesis, a decline in intestinal mucosal mass and, in post-menopausal women and some older men, an absence of estrogen or testosterone increasing bone resorption and decreasing renal and intestinal absorption (7, 10, 22, 23). Although calcium requirements increase, elderly individuals tend to consume less of nearly all nutrients including protein, energy, and calcium (3, 7, 9, 23).

Calcium is the principal cation of bone, and without sufficient intake, it is impossible to reach the genetic potential of the skeleton (21). Calcium balance is determined mainly by calcium intake (74). It is proposed that increasing calcium intake

over the life span will augment bone acquisition during growth, stabilize bone mass at maturity, and lessen bone loss during aging (8). Even a small decrease in the calcium reserve during the lifecycle correlates to a decreased bone mass and resultant decrease in bone strength (23). Calcium is lost every day through skin, hair, nails, perspiration, and waste excretion (10, 21), and if this loss is not counterbalanced by similar intakes from food, the body will take necessary calcium from existing structural units (8, 10, 21, 27). If this loss is not offset, blood calcium levels begin to fall, causing an increased secretion of parathyroid hormone, which results in resorption of calcium from bone (8, 43). Higher calcium intakes during childhood and adolescence are needed to increase the rate of bone accumulation and increase adult peak bone mass (PBM) (74, 75). Adequate calcium intake during adulthood and in the elderly is needed for bone maintenance and further protection against bone loss (7).

Calcium and Hip Fracture

A decrease in the size of calcium reserve leads to decreased bone mass, increased bone fragility, micro-architectural deterioration of the bony tissue and a decline in the strength of bone material resulting in osteoporotic fractures (23). Calcium is fundamental for the skeleton during growth, young adulthood and in old age, and a relationship exists between calcium intake and fracture risk in the elderly (76). By the year 2001, over 40 investigator control trials of calcium supplementation had been published showing significant benefit to bone health (23). In the elderly, that benefit was revealed as a reduction in age-related bone loss and lessened risk of fracture (23). Elevating daily calcium intake in individuals over age 65 may reduce osteoporotic fracture risk by from

30%-50% (23). The amount of calcium necessary per day is still uncertain for this population, although anti-fracture efficacy has been seen for intakes ranging from 1300 – 1700 mg/day (23).

Reduced fracture risk has been found in subjects given additional calcium (53, 55, 56, 77-80). Holbrook et al.'s results strongly support the hypothesis that increased dietary calcium among elderly subjects (ages 50-79 years) protects against osteoporotic hip fracture (79). In fact, the only factor consistently and significantly associated with risk of hip fracture was that hip fracture risk decreased as levels of calcium, in both men and women, increased (79). Although non-significant, Looker et al. found, using the First National Health and Nutrition Examination Survey (NHANES I), that the age-adjusted relative risk of hip fracture in the highest quartile of calcium intake was half of the lowest quartile among elderly individuals (80). Matkovic et al. found positive influences in both calcium supplementation and dairy product consumption in relation to BMD at the hip in late adolescent females (81). Heaney reported strong evidence from controlled calcium intervention studies that at higher calcium intakes, bone balance improved, bone loss decreased and fracture risk was reduced in the elderly (8). Seventy five percent of the observational studies reviewed by Heaney in relation to calcium intake resulted in positive effects on bone health (8). However, it is important to note that several studies (19 total) found no calcium effect on osteoporosis and fracture risk (8). Among this research were two prominent prospective studies: the NHANES-I Epidemiology Follow-up Study (80) and the Nurses Health Study (5). Similarly, Lanou et al. found that 27 out of 37 studies of dairy or unsupplemented dietary calcium intake

among children and adolescents had no relationship between dietary calcium intake and bone health (13).

Several other studies have shown no association between calcium intake and risk of hip fracture (33, 82-85). Cooper et al. found no change in risk of hip fracture in women consuming high amounts of calcium, but men with the highest intakes of calcium (>1041 mg/day) had significantly lower risk than controls (82). Wickham et al. and Tavani et al. also found no association with calcium intake and hip fracture among elderly men and women (84, 85). Dawson-Hughes et al. reported that calcium supplementation retarded bone loss in postmenopausal women at the radius and spine if calcium intake was previously below the RDA, but that there were no conclusive results in relation to the hip (56). Recently, further results were determined from the Nurses Health Study, re-confirming no association between calcium intake and fracture risk (54).

Opposing evidence is also available suggesting that, although high calcium intake has long been recommended for the prevention of osteoporosis, there is still insufficient evidence that recommended levels of dietary calcium successfully prevents osteoporotic fracture (70, 82, 86). Hegsted found that calcium can increase bone mineral content, but the changes had minimal effects on fracture risk (86). Hegsted's review also found the intake of calcium in most of the world to be low by American standards; yet these populations develop and perform well and without decreased bone health or signs of deficiency (86). Two studies done by the same group found that fracture risk in the elderly actually increased with higher calcium intake (36, 78).

It must also be noted that high calcium may decrease bone remodeling, and although bone remodeling can cause deleterious effects on bone, a certain amount is

necessary for the renewal of aging bone material and repair of microfractures (10). If this remodeling is suppressed below optimal levels for renewal and repair, bone fragility could increase. No data is available relating high calcium consumption to this biologically possible theory (10).

Calcium and Milk

Calcium is found in abundance in milk and other dairy products. About half of all dietary calcium intakes in North America are through milk consumption (87, 88). A retrospective study of postmenopausal women and milk intake in the early stages of life found that women who reported drinking milk with nearly every meal had a significantly higher average calcium intake than women who drank milk less frequently (89). Similar results were found in a publication associating childhood and adolescent milk consumption with calcium intake (47). Information from the USDA's Continuing Survey of Food Intake by Individuals found that drinking milk was positively associated with calcium intake (90). Women with osteoporosis have a significantly lower calcium intake derived from milk in comparison to total daily calcium consumption, which was only marginally lower than in controls (41). Among young girls, subjects consuming adequate amounts of calcium received the greater part of their calcium from milk as a beverage (91). These girls consumed almost two times the amount of milk daily in comparison to girls that did not receive adequate levels of calcium (91). Black et al. found a detrimentally lower amount of calcium intake among children who avoid drinking milk (87).

Diets low in calcium are also low in several other nutrients (2) that could be adequate if milk was present in the diet. Devine et al. found significant increases of several essential nutrients in the group receiving a milk powder supplement versus those receiving only calcium supplementation (3). Matkovic believes that calcium is beneficial to bone accumulation through influencing volumetric bone mineral density, while milk has additional properties and nutrients positively affecting bone growth and expansion (81).

Further research has shown that milk consumption has a significant effect on stimulating bone growth through increased IGF-I (2, 22), an effect that is not present from calcium supplementation or fortification (22). Increasing levels of IGF-I is considered to rise in response to the dietary protein provided via milk ingestion (22). This same effect is responsible for milks influence on bone metabolism and growth in newborn humans and animals (44). This evidence strengthens the hypothesis that milk's natural complex of components may have a greater effect on skeletal integrity than calcium alone.

Food sources have been shown to provide the most efficient and bioavailable way of obtaining the necessary calcium for bone health (40, 67). This is because bone health is not only affected by one nutrient, but several in conjunctions with each other. More evidence becoming available shows that the effect of calcium on bone may be dependent upon the status of several other nutrients (7). Milk not only contains calcium, but also vitamin D, phosphorous, protein, zinc, magnesium, lactose, and phosphopeptides formed from milk casein, all of which are important for bone health and calcium absorption in the intestine (7, 44).

Other calcium-rich foods such as almonds, broccoli, Chinese cabbage, tofu, collards, and mustard greens are not usually consumed consistently or in large amounts (67). A further issue for obtaining adequate calcium from non-dairy sources is bioavailability. Bioavailability is defined as "the amount of calcium available for use by the body and that is dependent, in part, on both the calcium load and substance in food that binds calcium" (67). Milk calcium is about 30% bioavailable (67, 69). Calcium bioavailability from plant foods can be inhibited through its content of phytate and oxalate (68, 69). An individual would have to consume eight cups of spinach to absorb the same amount of calcium available in one cup of milk (69). Calcium in other plant foods such as broccoli, kale, bok choy and sweet potatoes is highly bioavailable although not commonly consumed in a Western culture (68). Fortified juices and soymilk are other options of obtaining non-dairy sources of calcium (67, 68). Nutrient fortifications of these beverages are not standardized (67). The fortified juices provide similar levels of calcium and calories, but very few of the other important nutrients found in milk (67). Calcium absorption in soymilk has only 75% the efficiency of cow's milk (92). The last alternative is calcium supplements, which tends to add excess expense that many people cannot afford, and compliance with the use of supplements may be a problem (67, 68). Only one-fourth of American women, 14% of American men and 7.5% of young children (age 2-6 years) take calcium-containing supplements (68). It is also important to note that in a follow-up performed by Devine et al., milk powder compliance was significantly less than the calcium supplement (3). Compliance to fluid milk intake versus calcium supplementation or other food sources is unknown.

Milk consumption may be more beneficial to bone than calcium alone due to the density of other important nutrients and the high level of calcium bioavailablity from milk. Although this may be the case, most adults worldwide do not consume milk regularly and do not or cannot obtain the listed benefits.

Milk Avoidance

Milk avoidance at any time during life may be detrimental to older adults due to a possible insufficient calcium intake, thus increasing the risk of hip fracture. Reasons for milk avoidance are related to bad taste, soft drink availability vs. milk availability, concern about body weight, intolerance causing adverse effects, and family lifestyle choice (15, 87, 91, 93, 94). Milk consumption was affected by perceptions about milk and food habits in a population of Chinese adolescent girls (93). Half of the girls reported dislike towards milk, 5% reported that it was unavailable in the home, and an average of 18% stated feeling uncomfortable (upset stomach, cramps, bloating) after drinking milk (93). Black et al. found reasons for avoidance among children were related to intolerance (40%), bad taste (42%) and lifestyle choice (18%) (87). Hirota et al. found that 9.3% of the female Asian participants, 19-25 years old, avoided milk because they did not like the taste (94). In this particular study, 22% of the group of women with the lowest BMD did not drink milk during childhood, while significantly smaller percentages of the higher BMD groups did not drink milk during childhood (94). Fisher et al. found that girl's intakes of milk and sweetened beverages were associated positively with the beverage intake of their mothers (91). This similarity between mothers and daughters was statistically mediated by the frequency in which milk was served at meals and snacks

(91). A two-year observational follow-up study on Caucasian milk avoiders found that 65% of participants avoided milk because of lifestyle choices or taste dislike (15). The rest of the participants stated adverse symptoms were the cause of avoidance (15). These reasons for milk avoidance are all barriers to milk intake and may lead to osteoporotic fracture later in life.

Females tend to drink less milk than males (95). A survey performed by the USDA found a steep decrease in milk consumption in girls aged 14-18 years in comparison to females in the 4-8 year and 9-13 year age groups (90). The same decrease was not seen in boys (90).

Milk consumption frequency also seems to be lower in adulthood than in childhood (42, 96). Soroko et al. found that 19% of postmenopausal subjects reported drinking no milk during adolescence, whereas in midlife 28%, and in older adulthood 41% reported no milk intake (42). Sandler et al. found similar results, revealing that milk intake steadily decreases as women age (89). Although milk intake frequency tends to decrease as people age, research shows that women who drank milk regularly as teenagers were more likely to drink milk as adults (5, 97). This coincides with the results of Holbrook et al., finding that 95% of women reporting little or no milk intake as teenagers also drank little or no milk from ages 20-50, and 99% of women drinking little or no milk at age 20 drank the same amount after age 50 (97). Milk consumption in childhood can establish patterns of either milk consumption or milk avoidance that lasts throughout life (47, 98).

Obstacles to Milk Consumption

Total milk consumption in the United States continues to decrease slightly every year (11, 99). Milk intake has suffered because of misunderstanding about its content and has had relentless competition from soft drinks (16). Persons have decreased milk intake because of its fat content in relation to heart health and overweight issues (16) and possibly because of recent literature relating milk consumption to Type 1 diabetes (67). Heaney states, "the addition of milk to the typical Western diet results in overall dietary improvement and that this change can be accomplished without undesirable consequences for fat intake and only a small effect on body weight" (1). A study on milk supplemented, postmenopausal Asian women support this statement, showing an overall dietary improvement in subjects with low calcium intakes and no undesirable weight gain (4). Barr et al. concluded that three cups of milk per day, among men and women aged 55-85 years, enhanced nutrient intakes, reduced the prevalence of nutrient inadequacy in women, and did not seem to have substantive adverse effects on blood pressure, glucose level, or lipid metabolism, although a less than predicted elevation in body weight and triglyceride levels were noted (6).

Soft drinks are gaining popularity among children and adults as milk consumption continues to decrease (67, 100). Harnack et al. found that carbonated soft drinks may be a reason for milk avoidance or low milk intake because they displace milk in the diet (101). These beverages are high in energy but deficient in all other nutrients including calcium. In the last 20 years soft drink consumption has increased by 300% (100). Nielsen et al. gathered information about beverage intake in 73,345 subjects between 1977 and 2001 in the United States (99). Subgroupings for this analysis were by age

groups: children (2 to18 years), young adults (19 to 39 years), middle-aged adults (40-59 years), and older adults (60 years and older). Results for this study found that, in all age groups, sweetened beverage consumption increased and milk consumption decreased (99). Energy intake from sweetened beverages increase 135% overall and decreased from milk by 38% (99). All other beverage changes in these populations and age groups including coffee, tea, alcohol, fruit drinks and fruit juices were negligible (99). The proportion of subjects consuming soft drinks increased by about 15%, while those consuming milk decreased by 12% between 1977 and 1996 (99). The displacement of milk with carbonated beverages may result in calcium and other nutritional deficiencies, thus resulting in subsequent risk of osteoporosis and fractures.

Lactose Intolerance

The ability to digest lactose, the sugar in milk, is not widespread. About 30% of the United States adult population and 75% of the world's population are lactose intolerant (17). Lactose maldigestion was found to significantly affect more elderly women than young women, with 60% prevalence compared to 12%, respectively (96). Malabsorbers over 70 years old were also found to receive less of their total dietary calcium from milk than lactose absorbers (96). Lactose intolerance is also more prevalent among specific ethnic groups and in fact, adult tolerance is generally observed mostly among those with northern European descent (14). Several other lactose tolerant groups have been observed, for example; two nomadic pastoral African tribes, but these groups are always a minority among the human species (14).

Lactose intolerance is due to insufficient lactase, the enzyme that aids in the digestion of lactose. The undigested lactose travels through the large intestine where it is fermented by bacteria into gas and organic acids (67). The osmotic effect of water and the unabsorbed lactose, along with the resultant gas, is responsible for the symptoms of lactose intolerance (14, 67). Symptoms include bloating, abdominal pain and fullness, nausea, diarrhea and sometimes headache or fatigue (17, 67, 102, 103). The severity and nature of these symptoms are known to change, for better or worse, throughout life and have a variety of effects dependant upon the individual (103).

Individuals who avoid milk may or may not be lactose intolerant, although they often consider milk to be the cause of their gastrointestinal discomfort (95). Paajanen et al. found, in a population-based survey of young Finnish adults, most people claiming lactose intolerance or milk allergy self- diagnose themselves (95, 102). This blinded study found no difference in symptom outcomes comparing the cow milk group to a placebo soy drink group (95). Similarly, Carroccio et al. found, in an Italian population, gastrointestinal symptoms after lactose consumption were rare and that these subjects unnecessarily reduced their consumption of milk and had inadequate dietary calcium intakes (104). A double blind study in the United States, found that individuals with lactose maldigestion experienced minimal symptoms when consuming two cups of milk per day and may have mistakenly attributed their gastrointestinal discomfort to lactose intolerance (102). All of these studies were performed on generally lactose tolerant populations and results cannot be assumed for all ethnic populations (95, 102, 104).

Lactose malabsorption or intolerance in adults and children may be a barrier to obtaining essential nutrients through milk and milk products. The result of lactose

intolerance is the conclusion that milk avoidance is the most appropriate treatment (67). Elbon et al. found that among elderly subjects, 18% indicated milk intolerance and 57% of these subjects drank milk less than one time per month in comparison to the 22% of those that indicated tolerance (18).

Although this normal adult condition of lactose intolerance deters individuals from consuming milk, new evidence shows that the advantages of milk products may be accessible to these populations (40). Habitual milk drinkers can develop the intestinal flora and increase lactase activity necessary for digestion and absorption (14, 40). Johnson et al. found that African Americans between the ages of 13-39, with lactose intolerance, eventually adapted and tolerated milk with very little discomfort (105). Suarez et al. found that symptoms from lactose maldigestion are not major obstacles to the ingestion of a dairy rich diet, which supplies the 1500 mg of recommended calcium intake per day for elderly persons (17). About 50% of the women in this particular study, from both the control group and the lactose maldigestion group, indicated that they preferred obtaining the recommended calcium from the consumption of dairy and milk products instead of calcium supplements (17). Further study should be performed to find and develop ways to increase tolerance of milk (105), thus providing more options for lactose intolerant individuals to increase calcium and several other key nutrients in the diet.

Milk Avoidance and Bone Health

"All patients with diseases involving total or partial withdrawal from milk products for a prolonged period are a group at potential risk of defective bone

mineralization" (106). Recent studies have found that children who avoid milk have shorter stature, smaller skeletons, lower total body bone mineral content, and lower bone mineral density at the femoral neck and hip trochanter (107). Young children (age 3-13 years) who avoid milk experienced more total fractures than the rest of the cohort being studied (107). Five studies performed in different countries have all shown low BMD and low total calcium intake in children with a chronic history of milk avoidance (87, 106, 108-110). A study on Chinese adolescent girls split the subjects into three groups based on milk consumption: no milk, low milk (less than the median), and high milk (greater than the median). The "no milk" group had the lowest BMD and the "high milk" group had the highest BMD (93). A study of children on "milk-free" diets secondary to milk allergy found decreased bone mineralization (110). The children in these studies, lacking the essential nutrients needed for bone growth, also experienced (107) or were at risk for a greater number of fractures (15).

Lactose malabsorption does not directly affect the rate of bone loss or risk of osteoporosis unless there is a reduction in calcium because of milk avoidance due to discomfort and conditions associated with malabsorption (96, 111). A study done on postmenopausal women found that low milk consumption, due to lactose intolerance and malabsorption, contributed to an increased risk in developing osteoporosis (41). Honkanen et al. examined lactose intolerant women with long-term low intake of calcium and found a reduction in milk intake of 33% compared to those in the control group (111, 112). Among this same group, total fracture risk was significantly higher in those with lactose intolerance compared to other women (111). A study on perimenopausal Finnish women found a reduction in dairy calcium among lactose intolerant subjects secondary to

their reduced consumption of fluid milk (112). There was also a reduction in femoral BMD in which dairy calcium intake was an independent factor (112). Research has found a greater prevalence of lactose malabsorption and intolerance among osteoporotic subjects, (111-114) most likely due to a decreased consumption of milk products and total calcium intake and not directly due to the condition of malabsorption.

Peak Bone Mass

Peak bone mass (PBM) is the highest level of bone mass achieved as a result of normal growth, and before the seemingly unavoidable bone loss that occurs with age (27). The accumulation of bone mineral density during adolescence is more than double in magnitude compared to bone loss during the rest of life (76). About 40% of PBM is accrued during adolescents (100, 115). PBM seems to be reached from ages as early as 14 or 15 in females and 17 or 18 in males to as late as 35 years (2, 27, 43, 116, 117). Bonjour et al. found no further bone acquisition after age 18 in a cross-sectional study of 207 boys and girls (117). In another cross-sectional model, Matkovic et al. found that the bone density of the hip peaks at age 18 and slowly declines for the rest of life (118). A different study by Matkovic found that girls, by the age of 16, had gained 90 – 97% of the bone mass of their premenopausal mothers (74). A longitudinal study was performed during the female pubertal years to determine the crucial years of skeletal mass accumulation, which found the rate of increment was distinct from the ages of 11- 14 (119). Statistical significance was lost and rate of increment fell considerably after age 16 and/or two years after menarche (119). Rate increment in BMD in males was distinct

from ages 13 - 17 and markedly declined thereafter in the femoral neck (119). Teegarden et al. determined total peak BMD to occur by the early 20s (116).

BMD and rate of bone loss later in life can be determined by an individual's PBM attained in youth (118). Once bone loss begins, it proceeds at a rate of about 6-8% per decade, resulting in a cumulative deficit of about 30-40% by 70 years of age (120). Therefore, PBM may be an important factor in determining risk of or resistance to fracture later in life (2, 27).

Primary prevention of osteoporosis and hip fracture consists of accumulating the largest peak bone mass possible within the limitations of the genetic possibilities (2, 27, 30, 89). Much of this necessary bone accretion is due largely to genetic factors and in a smaller degree to hormonal, nutritional, and environmental factors (30). The genetic program is not alterable, but nutrition is modifiable and plays an integral role in influencing skeletal mass. Nutritional factors impacting bone health include energy, protein, and vitamins and minerals (27, 74, 94). Nutrition deficiencies will restrict bone growth and limit achievable PBM (8, 27, 29). Because nutritional factors can be improved through milk consumption, this beverage may positively influence bone mass and help fulfill the genetic potential of skeletal strength.

Milk Intake at Time of Peak Bone Mass and Risk of Hip Fracture

Childhood and adolescent milk consumption is not only beneficial for growth and development, but is also helpful in obtaining optimal PBM and greater potential of skeletal integrity throughout the aging process (89). Teegarden et al. found that higher milk intake during childhood and especially adolescence is associated with greater total

body BMD during the development of PBM (47). Bone mineral accumulation, during an 18 month clinical trial in girls around the age of 12, was significantly higher in the group given milk supplements verses those in the control group (2). As previously mentioned, a study done on BMD by milk consumption groups in Chinese adolescent girls found that the "high milk group" had the highest bone mineral density and the "no milk group" had the lowest (93). No other dietary variables, other than milk intake, were able to explain the difference in BMD (93). Du et al. suggests that the positive effect of milk on bone mineral is most likely due to an "integrated consequence of its provision of several nutrients" (93). Nutrients that revealed positive correlations with bone measurements included vitamin D, calcium, and protein (93). Hirota et al. found that current intakes of protein, energy, and calcium were significant dietary factors contributing to BMD (94). The nutritional density of these important nutrients found in milk, suggests that high milk consumption in childhood will increase PBM (94).

Relatively few studies have shown a direct link between milk intake during adolescents and later osteoporotic risk (75). Most studies examining childhood and adolescent milk intake in relation to BMD and fracture risk later in life have relied on recalled data, and results have been inconsistent (75).

Although milk consumption data was obtained from recall through retrospective studies, some positive associations with PBM and fracture risk have been found. Sandler et al. found significantly higher bone densities in postmenopausal women who reported drinking milk with every meal in comparison to women who reported drinking milk less frequently during childhood and adolescence (89). Soroko et al. found significant associations between milk intakes and later bone health determinants, which were

strongest during midlife (20-50 years of age) (42). Another study found that teenage milk consumption was significantly associated with higher BMD in white women ages 20-39 and in white postmenopausal women, but was not associated with the bone mineral density among black women (98).

Adequate PBM accumulation may decrease risk of or postpone occurrence of osteoporotic hip fracture. A 5% to 10% insufficiency of PBM may consequently result in a 50% greater lifetime prevalence of hip fracture (100, 115). Milk intake has a useful effect on bone mass, which, if sustained throughout adolescent growth and into adulthood, could favorably modify attainment of PBM and further delay bone loss and decrease fracture risk (2, 88, 89, 98). Data from NHANES III found that women, aged 20-49 years, consuming less than one serving of milk per week during childhood and adolescence had a hip bone mineral content that was 5.6% and 3%, respectively, lower than those consuming greater than one serving of milk per day ($P < 0.01$ and 0.02) (121). This same study found a significant association of milk consumption and hipbone mineral content and BMD in women older than 50 years (121). Similarly, regular milk intake before age 25 is associated with higher hip BMD in middle aged and elderly women and may decrease the risk of hip fracture later in life (88). Accrual of PBM in relation to hip BMD was about 5% greater among women reporting the most frequent milk consumption compared with least frequent milk consumption at all hip sites (88). Low milk intake during both childhood and adolescence has been associated with a two-fold increase in lifetime risk of hip fracture (121). Teegarden et al. found significant differences between premenopausal women (45-49 years) who reported a low intake of milk (under one cup per day) in their childhood and adolescence and those reporting medium or high intakes

(1-2 cups per day and more than 2 cups per day, respectively) in relation to BMD of the spine and hip trochanter (47).

The role of milk intake during PBM accrual on later risk of osteoporotic hip fracture is still inconclusive. Nieves found no relationship between milk and calcium intake during the teenage years and risk of hip fracture (49). The Nurses Health Study, both at the 12-year and 18-year follow-ups, found no association between reported milk intake during adolescence and risk of fracture (5, 54).

Bone maintenance is a lifelong concern, especially for developing PBM leading to the prevention of age related bone loss in the elderly. Ingestion of milk during childhood and adolescence may be a beneficial dietary way of obtaining optimal bone health. Unfortunately, the study of beverage consumption between 1977 and 2001 by Nielsen et al., showed the largest drop in milk consumption occurred in the 2 to 18 year old age group (99). A total energy decrease from 13.2% in 1977 to 8.3% in 2001 from milk was found among this age group (99). At this same time, total energy intake from soft drinks increased from 3.0% to 6.9% (99). The number of milk servings decreased in the child and adolescent groups from 3.46 servings per day in 1977 to 2.85 servings per day in 1996 (99).

Pregnancy

During pregnancy a significant transfer of calcium may occur from the bones of the mother to the fetus, thus decreasing the bone mass of the mother (122, 123). Approximately 50 mg/day at 20 weeks of gestation and about 330 mg/day at 35 weeks are provided to the fetus from the pregnant mother (76, 124). This theoretically places

the mother at an increased risk of osteoporosis and hip fracture later in life, especially if there were no efforts to maintain calcium levels during pregnancy (10, 76, 125). Calcium lost through the noted transfer may be replaced by consuming high levels of calcium through milk and supplements (124, 126). This suspicion has not been verified, and studies have shown that calcium absorption and excretion during pregnancy is associated more with hormones and changes in calcium homeostasis than with maternal diet during pregnancy (122, 124-127).

Maternal Bone Status and Pregnancy

Bone resorption is increased during pregnancy in comparison to pre-conception (124). Bone turnover rates increase by 50% - 200% during the gestational period (124). Throughout pregnancy there has been found a loss of maternal BMD of around 5% (76, 128). Drinkwater et al. found a significant reduction in BMD in the femoral neck during pregnancy (129). Hreschyshyn et al. had similar findings and determined that femoral neck density decreased by about 1.1% per live birth (130). A more recent study found a 1.15% significant decrease in BMD of the total hip during pregnancy, but not at the femoral neck (131). Although bone mass has been shown to decrease during the third trimester, a full recovery can usually be expected after delivery (123, 125, 131, 132). Lamke et al. found a decrease in the trabecular bone of the hip, during pregnancy, but six months after delivery the bone mineral content did not differ from the controls (133). Other studies have found no significant association between pregnancy and decreased BMD (76, 122, 125, 132, 134-136).

Perhaps the female reproductive history and its association with decreased BMD during pregnancy are associated with risk of osteoporosis and fracture. As noted above, uptake and release of calcium from the skeleton occurs during pregnancy. Changes occur in the bone mineral content of the mother, and these changes may alter the risk of osteoporosis later in life if bone changes are of sufficient magnitude (137). Ramalho et al. found that a group of women with proximal femur fracture experienced significantly more pregnancies than the control group without proximal femur fractures (138). In contrast, Cure-Cure et al. reported that post-menopausal women with two or more deliveries had an 8% higher BMD of the femoral neck and a 3% higher total body BMD than nulliparous women (139). Michaelsson et al. found a 5% lower hip fracture risk per child delivered (128). A "low number of pregnancies" was found to be an independent factor among Asian women and supports a protective role of high parity for hip fracture (140). Hoffman et al. also found that a reduction in the risk of hip fracture was associated with ever having a live birth. (141). Wengreen et al. found that among parous women, those with hip fractures had fewer live births than controls (142). A cross-sectional study and a prospective study found that having no children was associated with a higher risk of hip fracture compared to having at least one child (143).

Other studies show that parity is not associated with a decreased risk of osteoporosis and hip fracture later in life. A case-control study found that women who experienced pregnancy four or more times had similar fracture risk compared to women who had never been pregnant (134). A review by Ensom in 2001 found no association relating a greater number of pregnancies to a greater decrease or increase in BMD (123).

Few studies have taken into account pre-natal diet in association to bone health later in life. Also, limited research is available comparing dietary intake among women who have been pregnant to show whether an increase of milk consumption or calcium during pregnancy has a protective effect on the incidence of hip fracture.

Maternal Calcium Intake and Pregnancy

The effects of dietary or supplementary calcium during pregnancy are uncertain because of the lack of information on this topic. Few studies have been performed to determine the impact of maternal calcium or milk consumption on bone mineral changes during pregnancy and the effects during late adulthood. Accumulating data suggests that bone changes during pregnancy are independent of maternal dietary calcium intake (125, 137). Most studies to date have used well-nourished subjects that actually exceed current calcium recommendations of 1200mg/day (124, 144). Sowers et al. found no influence of calcium intake during pregnancy on altered bone mineral content in American women consuming between 1100-1350mg per day (122). Drinkwater et al. found a significant decrease in bone mineral density at the femoral neck even when the study subjects were consuming calcium in excess of the current RDA (129). Ritchie et al. held calcium intake constant at around 1200 mg/day in a study of 14 well-nourished women and found that true calcium absorption increased from 33% at pre-pregnancy to 50% in the second trimester and 54% in the third trimester (126). These study results show that pregnancy-associated changes in calcium and bone metabolism do occur, even in women with optiaml calcium intake (124, 137).

Socioeconomic and cultural factors may keep pregnant women from consuming their physiological calcium needs of 1200 mg/day, thus compromising their BMD (138). At the postmenopausal period, calcium deficiency during pregnancy may increase the risk of hip fracture (138). This theory has no evidence to provide legitimacy. Ramalho et al. found no association between dietary calcium intake and protection from proximal femur fracture, even in women with very low intake (138). Low-income pregnant women were supplemented 300 mg and 600 mg of calcium daily during the last 20 weeks of gestation. Although a significant increase in the bone density of the infant was found, no difference was observed between initial and final bone densities among the mothers (145). Another study looking for a relationship between pregnancy and bone mass detected no correlation between changes in bone mineral content and milk consumption (133). General intervention during pregnancy has little or no effect on bone loss, even in cases with an already low nutritional intake of calcium (76, 124). These results lead to a conclusion that dietary intake during pregnancy is not related to maternal bone content, and the high demands of calcium for fetal growth is provided by physiological means including increased intestinal calcium absorption and increased rate of bone turnover (76, 124, 133, 144). If justified, more research should be performed looking for a relationship of dietary intake, particularly milk intake, during pregnancy and risk of hip fracture later in life.

Late Adulthood

Osteoporosis most often presents after a person is 50 years old, and a dramatic rise in the incidence of hip fracture occurs after age 65 years (26). White women over 50

years have a 16% lifetime risk of suffering from a hip fracture and white men have a 5% lifetime risk (146). As previously mentioned, bone loss slowly progresses over time, increasing bone vulnerability in older adults (7). Because of the occurrence at a later time in life, consideration and prevention of osteoporosis is often postponed. Evaluation of the evidence from NHANES I found that women, aged 55- 74 years, who suffered from subsequent hip fracture had poorer dietary intakes including significantly lower levels of total energy, carbohydrate, protein, and phosphorous intakes and marginally lower calcium intakes than those women without hip fracture (39). An estimated 20% of elderly individuals in the United States regularly consume less than 60% of the RDA for either phophorus, protein, or both (52). This low level of dietary protein intake has been associated with a significant risk of hip fracture in a study done on elderly men and women of Utah (51). Wengreen et al. found a 65% reduction in hip fracture risk among elderly consuming the highest amounts of protein (51).

Increasing calcium, protein, and other important nutrients, through the consumption of low fat milk and dairy products, may help reduce age associated bone loss. Elbon et al. stated that "failure to consistently consume the recommended two or more servings of milk products per day is a major health indicator of low calcium intakes and poor nutritional status in older people and is associated with an increased risk of osteoporosis" (18). Increasing milk intake may be difficult for the elderly because total food and energy intakes have been shown to decrease with age (3), which is also seen in amounts of milk consumption (42, 89). Reasons for this reduction is unknown but suspected to be secondary to health problems and decreased appetite (3, 42).

Milk Intake in Late Adulthood and Risk of Hip Fracture

Nutritional benefits of milk consumption during late adulthood may still be effective in decreasing fracture risk (1, 4, 42, 97, 147). Chee et al. found a significant decrease in the percentage of bone loss at the femoral neck and total hip by supplementing the diet of postmenopausal Chinese women with two cups of high calcium milk (4). This decrease in bone loss may not only be due to the high calcium in the milk supplements, but also due to the increased intakes of vitamin D, protein, magnesium and zinc (4). Low consumption of milk and hard cheeses has been found to be a risk factor for hip fracture in men older than 50 years in Europe (31). An 18-year prospective study focusing on increasing baseline 24-hour dietary calcium from milk and food intake in men and women aged 45 years or older found an independent, significant increase in bone mineral density in the femoral neck ($p < 0.01$) and total hip ($p=0.05$) in women (97). The same effect did not prove significant in the hip site of men (97). Soroko et al. found that with higher milk consumption in adulthood, there was an independent and significant association with higher BMD at the total hip, trochanter, and intertrochanter (42). Findings in female patients, aged 50 years and over, in the Thai population support the role of both milk and calcium intake on hip fracture prevention (140). This case-control study found that "not taking milk regularly" and "low serum calcium" were independent risk factors for hip fracture (140). Johnell et al. identified low milk consumption as a significant risk factor for hip fracture in the lowest 10% of milk intake among women aged 50 years and older (34). High calcium intake in the form of milk was also associated with a significantly lower risk of hip fracture (34). Recker et al. found that in

healthy postmenopausal women, those receiving 24 ounces (3 cups) of milk per day had significant beneficial effects on calcium absorption and bone accretion, and concluded that milk can be recommended as a good source of calcium in relation to bone health in the elderly (45). Heaney et al. performed a study on 204 men and women aged 55 – 85, who regularly consume less than 1.5 servings of dairy food per day (1). Participants in the intervention group added 3 cups of milk to their regular diets, which resulted in a 13% decrease in bone resorption (1). After 18 months of receiving supplementation of vitamin D and calcium, both of which have been shown to increase with regular milk intake (6), Meunier et al. found that bone density had increased by 2.5% from baseline, and actually decreased by 4.6% in the placebo group (147). Prince and Devine, in a 2-year randomized placebo-controlled study, found that calcium supplementation through milk powder or calcium supplements retarded bone loss at the hip site in 168 postmenopausal women (148).

Other studies have shown no association between milk consumption during late adulthood and hip fracture risk, whether protective or detrimental (5, 85, 88, 149). The 12-year and 18-year Nurses Health Study follow-ups show that high milk consumption (>2.5 cups per day) and high calcium intake in women over age 50, slightly reduced risk of hip fracture although not significantly (5, 54). Michaelsson et al. found no association between consumption of both dietary calcium and vitamin D in a prospective cohort of women aged 40 – 74 years and prevention of osteoporotic hip fracture (149). In a case-control study of postmenopausal women, Tavani et al. found no significant association with milk, using individuals with a milk intake of less than 7 cups per week as a reference group in comparison to 7 cups per week and 7 or more cups per week (85).

The evidence of a relationship between hip fracture and milk intake in the elderly is unclear possibly because of misclassification errors, sampling variation, recall ability and because many of the studies focus only on calcium intake verses the total food effect (97).

Conclusion

Milk is strongly advocated and marketed as a beneficial food for bone health, although results have not supported this assumption. A review of the literature shows inconclusive results in relation to milk intake at specific stages in life and risk of hip fracture.

Although the nutritional content of milk is well understood and the product is easily attainable and inexpensive (1), most of the world's adult population does not drink milk due to physiological reasons and personal choice.

Milk is a good source of calcium, phosphorus, energy, and protein, all of which are important for achieving optimal peak bone mass. Skeletal mass acquired during adolescence and early adult life is an important determinant for osteoporosis in the elderly. Appropriate nutrient intake at a young age is important for obtaining the highest PBM possible within genetic limits.

Milk can help attain appropriate calcium intake necessary for optimal fetal development but, based on current research, recommendations cannot be made about milk intake during pregnancy and decreasing risk of osteoporotic hip fracture.

As people age, food intake decreases, even though specific recommendations for vitamins and minerals increase. Undernutrition is a common problem among individuals

suffering from hip fracture. Being as milk is an efficient food for increasing essential nutrients in the diet, it may be helpful in improving overall nutrition and decreasing hip fracture risk.

Further research and statistical analysis on milk consumption in association to hip fracture may have important public health implications. Information will be advantageous to individuals and the health care system if the amount of milk consumed during a particular stage of life proves more helpful than another. This information can also trigger more research to be done on milk consumption in relation to osteoporotic hip fracture.

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CHAPTER III

MILK INTAKE IN EARLY AND LATE ADULTHOOD AND RISK OF OSTEOPROTIC HIP FRACTURES IN UTAH[1]

Abstract

The relationship between milk intake and risk of osteoporotic fractures is uncertain. Associations between milk intake and milk avoidance in relation to osteoporotic hip fracture were examined in the Utah Study of Nutrition and Bone Health (USNBH), a statewide case-control study. Cases were ascertained at Utah hospitals treating 98% of hip fractures during 1997-2001 and included 1188 men and women aged 50-89 years. Age- and gender-matched controls were randomly selected from Utah driver's license and Medicare databases (N= 1324). In-person interviews were conducted and participants reported frequency of milk intake per week at age eighteen and during pregnancy among women who reported being pregnant. Milk avoidance for a period of more than one year and duration of milk avoidance was also reported. Diet and supplement intake in the one-year period before fracture (cases) or the interview (controls) was assessed using a picture-sort food frequency questionnaire. Milk consumption frequency was categorized into four levels of intake at each life stage. Total calcium intake was categorized into quintiles of distribution of intake. Logistic regression models were used to examine associations between milk intake and milk avoidance and risk of hip fracture while controlling for the potential confounding effects of gender, age, body mass index, alcohol use, smoking, physical activity, estrogen use,

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and total calorie, protein, calcium and vitamin D intake. Recent milk intake, milk intake during pregnancy and milk avoidance duration were not associated with risk of hip fracture. A borderline association was found at age 18 showing a decreased risk of hip fracture among those in the highest quartile (≥ 15 cups of milk per week) of milk intake (odds ratio (OR): 0.86, 95 percent confidence interval (CI): 0.75, 1.00; P = 0.046). Milk avoidance for a year or more was associated with an increased risk of hip fracture compared to those who did not avoid milk (OR: 1.38, 95 percent CI: 1.07, 1.78). A significant interaction was found between milk avoidance and quintile of total calcium intake (P = 0.02). Milk avoidance was associated with a significantly higher risk of hip fracture at the lowest two quintiles of calcium intake (OR: 1.72, 95 percent CI: 1.26, 2.17; P = 0.02 and OR: 1.58, 95 percent CI: 1.01, 2.15; P = 0.01, respectively) but was not associated with elevated risk among those with higher calcium intakes. In conclusion, milk intake during pregnancy for women, and in the year before hip fracture (for cases) or before interview (for controls) was not associated with hip fracture risk. The highest level of milk intake at age 18 was associated with decreased risk of hip fracture. Avoidance of milk for one year or more was associated with hip fracture risk, but only among those with low calcium intake (Q1 and Q2).

Introduction

Hip fracture is the most devastating fracture resulting from the destructive bone disease, osteoporosis. This disease, characterized by low bone mass and micro-architectural alterations which leads to fractures, occurs in both men and women and is a serious global health concern (1, 2). Osteoporosis is a multi-faceted disease and no single

intervention, whether medicinal, hormonal or nutritional, can completely solve the problem of bone loss and associated hip fracture (3). Bone mass is dependent upon a number of different variables, which include genes, hormones, race, gender, exercise, body weight, disease, medical treatments, and nutrition (3, 4). These factors contribute to bone loss and osteoporosis through influencing bone mass accumulation during growth and bone mass maintenance during aging (3, 5).

Nutrition is a modifiable variable in relation to osteoporosis and may lead to a decreased prevalence of hip fracture. Prevention of bone loss through diet is complex and involves many nutrients (6). Hip fractures are most commonly found in individuals with numerous levels of dietary deficiencies (3). Nutritional improvement has been achieved by increasing milk in the diet, and may result in a decreased risk of hip fracture (7-12).

Milk contains calcium and other important nutrients needed for bone health including protein, phosphorus, magnesium, zinc, riboflavin, thiamin, vitamin B12 and energy (6, 13-26). Because milk is more commonly consumed than other dairy in the United States (27) and its nutritional content is well understood it can be considered a good food to study in association with osteoporosis and hip fracture. Milk is also heavily marketed as beneficial for skeletal health and is of interest since related research is inconsistent (3, 28, 29). Although the essential nutrients found in milk may work to sustain bone growth and maintenance and lead to dietary prevention of hip fracture (3), most adults worldwide cannot tolerate this beverage or choose not to drink it for various reasons (30-34). Furthermore, the research has shown unconvincing results on the role of milk in relation to hip fracture

More insight is necessary to provide recommendations for milk intake throughout the lifecycle. The amount of milk consumed during particular stages of life, such as adolescence, pregnancy, and older adulthood, may prove more beneficial than another stage (28, 29, 35). The associations between milk intakes at these specified stages, milk avoidance and milk avoidance duration, and risk of osteoporotic hip fracture were explored in the elderly population of Utah.

Subjects and Methods

Study Participants

The Utah Study on Nutrition and Bone Health is a statewide case-control study performed to collect data on risk factors for hip fracture in the elderly, ages 50 to 89 years, during years 1997 and 2001. Patients were identified through review of medical records in 18 hospitals that were involved in the treatment of 98% of all hip fractures in the state of Utah. The total number of hip fracture patients during the targeted years was 3,701. An average of 4.2 months after their fracture 1,366 individuals, identified as cases, were interviewed. Control subjects (n=1,368) were randomly selected from the Utah Driver's License and Medicare databases and matched to the cases by gender and five-year age intervals. Control subjects were also interviewed. The Institutional Review Board of each hospital and Utah State University approved all study protocols.

Similar numbers of cases and controls refused the interview (23.3% and 24.0%, respectively). More cases than controls were incapable of completing their interview due to frailty, illness or death (37.2% and 16.8%, respectively). 2.8% of cases and 3.4% of

controls were unable to be located. The overall participation rate was 36.9% of cases and 55.8% of controls.

Data Collection

Information collected during the in-person interview was based on self-report from each individual and occurred at either the participant's place of residence or assisted living center. Supplement use, medical history, family medical history, fall history, history of previous functions, cognitive function, pharmacology, levels of physical activity and historic diet intake were all reported in the interview. Subjects were asked to recall how often per week they consumed an 8-ounce glass of milk at age 18 and during pregnancy for women who reported being pregnant. Participants were also asked to recall if there was ever a time that they avoided milk for a year or more, for any reason. If this answer was affirmative the duration of milk avoidance was reported.

Dietary intake at the time of the interview for controls and time of hip fracture for cases was ascertained with a 137-item picture-sort food frequency questionnaire (FFQ) (17). This FFQ was specifically developed for the elderly Utah population being studied. It was used as an alternative to the more often used paper and pencil format and was designed to help elderly respondents who often have problems with memory, vision or hearing to more accurately report their usual dietary intake. The foods included in this particular FFQ were systematically chosen from the 126-item Nurses' Health Study FFQ, the National Cancer Institute FFQ, and a list of commonly eaten foods identified in focus groups of the elderly in Utah. The picture-sort FFQ method used a two-step process. The first step involved having respondents sort food cards with color photographs into

trays representing frequency of use over the past year, for controls, or the year prior to hip fracture, for cases (17, 36). In the second step the respondent reported their actual frequency for foods within each frequency period (day, week, month, etc). This dietary assessment was found reproducible on repeated administration and validated when compared to 24 hour dietary recalls (17).

Several exclusions were used prior to statistical analysis. Interviews of participants 90 years and over were discontinued and excluded because of high levels of frailty (n=34). Hip fractures that occurred secondary to a high-impact trauma, such as motor vehicle accidents or falls from higher than standing height, were excluded (n=117). The Mini-Mental State Examination (MMSE) was used to measure cognitive function and each MMSE score was adjusted for sensory impairment. Participants with an adjusted MMSE score of 17 or less, an indication of severe cognitive impairment were excluded (n=33). Improbable total energy intakes of less than 600 or greater than 5000 calories were not included in the analyses (n=44). In models of milk intake at age 18 and during pregnancy, study participants with unlikely milk intake of greater than 12 servings per day were excluded (n= 24, 3, respectively). All men and any woman who had never been pregnant were not included in models referring to milk intake during pregnancy (n= 780, 124, respectively). The final hip fracture case group contained 1187 individuals, 854 women and 333 men. The final control group contained 1324 individuals, 877 women and 447 men.

Statistical Analysis

Descriptive analyses were carried out to compare the characteristics and milk intake variables between case and control subjects. Further analyses were done to observe characteristics of milk avoiders and non-avoiders. Analysis of variance (ANOVA) was performed to assess the differences in means among continuous variables. Differences between categorical variables were compared through χ^2 tests.

Logistic regression analysis, with case-control status as the dependent variable, was used to evaluate the associations between lifetime milk intake, lifetime milk avoidance and hip fracture. To facilitate analysis the milk intake variables were collapsed into four categories: 0-1 cups of milk/ week, 2-7 cups/ week, 8-14 cups/ week, and >15 cups/ week. Milk avoidance status (yes or no) was included as a categorical variable. Quartiles of milk avoidance duration was also observed: $\leq$ 6 years, 7-25 years, 26-63 years, and $\geq$ 64 years. The lowest categories of milk consumption and avoidance duration were used as reference variables.

Potential confounding variables known to affect hip fracture were included in the logistic regression models. These variables included gender, age, weight, height, body mass index (BMI), alcohol consumption, smoking history, physical activity, estrogen use, total calcium and vitamin D intake, total calorie intake, and total protein intake. Age was categorized into three groups: 50-69 years, 70-79 years, and 80-89 years (37). Smoking and alcohol variables were labeled as never, former or current users; both covariates were related to risk of hip fracture and included in the models. Estrogen use and sex were included in the models by coding four levels: women who never used estrogen, women who formerly used estrogen, women who currently use estrogen and males. A significant

result was found in the association of BMI with milk avoidance, therefore BMI is a potential confounder and is included in all models. Physical activity was included due to the association with risk of hip fracture and was labeled as either none, one, two or three moderate physical activities per day. Total calorie and protein intakes were determined from the FFQ. Total calcium and vitamin D intake amounts were determined from the sum of dietary intake obtained from the FFQ, as well as from the individual, multi or combination vitamin use obtained from the interview.

Milk avoidance was significantly associated with increased risk of hip fracture ($P= 0.01$). Interactions terms for milk avoidance with other variables were included in the multiple logistic regression models in order to determine if the effects on hip fracture rate was dependent on milk avoidance status. Statistically significant interactions were found between milk avoidance status and the sum of both total calcium intake and total vitamin D intake. Through further investigation calcium and vitamin D intake were categorized into quartiles and quintiles. Categorized variables of total vitamin D intake held no association with milk avoidance and hip fracture. Quintiles (Q) of total calcium intake (Q1; $\leq$ 860 mg/day, Q2; 861-1200 mg/day, Q3; 1201-1563 mg/day, Q4; 1564-2085 mg/day, Q5; $\geq$ 2085 mg/day) were significantly associated with status of milk avoidance and risk of hip fracture ($P= 0.02$). Odds ratios for hip fractures were computed and compared for all combinations of milk avoidance and total calcium quintiles relative to non-milk avoiders at the lowest quintile of total calcium intake. Further contrasts of odds ratios for hip fracture comparing milk drinkers to milk avoiders within each quintile of calcium intake were examined.

All analyses were accomplished through SPSS software, version 11.0 (SPSS, Chicago, IL, USA) and SAS software, version 8.0 and 9.1 (SAS Institute, Cary, NC, USA).

Results

The characteristics of case and control participants were compared in Table 1. The study population was 97.3% non-Hispanic white. Participants with hip fracture, among both men and women, weighed less, were taller, had lower mean BMI, and were less physically active compared to controls. Among women, more cases than controls had never taken estrogen other than for contraception, had ever smoked and had regularly used alcohol in their lifetime. Among women who reported being pregnant (n= 1605), mean intake of milk was significantly lower in cases than in controls. Also, significantly more female cases reported avoiding milk for a year or more at any time during their life compared to controls. Similar results were seen among men in relation to both milk avoidance and smoking, although not significant. There was no significant difference in age, calcium or vitamin D intake, and milk avoidance duration when comparing cases to controls.

Table 2 includes characteristics of milk avoiders and milk drinkers by case control status. Among controls more milk drinkers had never smoked and more milk avoiders were former smokers. Among cases milk drinkers were older than milk avoiders. Neither gender, estrogen use, regular alcohol use, physical activity, height, weight or BMI showed a significant difference between milk avoiders and milk drinkers among case and control groups. Among cases, means of both calcium and vitamin D intake in

milk drinkers were significantly higher than those of milk avoiders. Milk drinkers with hip fracture also consumed significantly more calories, total protein, animal protein and total fat than milk avoiders. Among controls, milk drinkers had a significantly higher vitamin D intake, total protein intake and animal protein intake. Milk avoiders in both the case and control groups drank significantly less milk than milk drinkers at age18, during pregnancy for those who had been pregnant, and at the time of hip fracture for cases and time of interview for controls. Among both the cases and control groups more milk avoiders chose to also avoid other dairy foods for a year or more. There were no other associations observed when exploring avoidance of foods such as red meat, eggs, turkey or chicken.

Significantly less amounts of milk were consumed at the time of interview compared to the amount of milk intake at age 18 and during pregnancy ($P \leq 0.001$). This difference was seen for both cases and controls (Table 1) and for milk avoiders and milk drinkers (Table 2). Although this decrease was highly significant among all groups, an especially large decrease in milk consumption was seen among milk avoiders (Table 2).

Tables 3, 4, and 5 reveal unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) by level of milk intake at age 18, during pregnancy among women who reported being pregnant, and the time of interview for controls and time of hip fracture for cases, respectively. A borderline significance was seen between the highest level of milk intake at age 18 and risk of hip fracture (OR: 0.86, 95% CI: 0.75, 1.00; $P = 0.046$). No association to risk of hip fracture was found at any level of milk intake during pregnancy or older adulthood.

A significant increase of hip fracture risk among milk avoiders versus milk drinkers (both crude and adjusted) is shown in Table 6 (OR: 1.45, 95% CI: 1.14, 1.83; P = 0.0021 and OR: 1.38, 95 % CI: 1.07, 1.78; P = 0.014, respectively). Quartiles of milk avoidance duration, as seen in Table 7, held no significant association in relation to hip fracture risk.

Table 8 describes the interaction between milk avoidance and quintile of total calcium intake in relation to risk of osteoporotic hip fracture. Figure 1 demonstrates the interaction described in Table 8. The table and coinciding graph show a higher risk of hip fracture among milk avoiders in the lowest two quintiles of calcium intake compared to milk drinkers in the lowest quintile of calcium intake (OR: 1.72, 95% CI: 1.26, 2.17 and OR: 1.58, 95% CI: 1.01, 2.15, respectively). Reported P-values were found by comparing odds ratios within each quintile of calcium intake. Milk avoiders in the lowest two quintiles of calcium intake had an increased risk of hip fracture compared to milk drinkers consuming similar amounts of calcium (P = 0.0196 and 0.0132, respectively). For the highest three quintiles the differences between milk avoiders and non-avoiders were not statistically significant.

Discussion

Milk consumption at the age of 18 years, an important time of PBM accrual (38-42), was found to be slightly significant in relation to risk of hip fracture among those consuming 15 or more cups of milk per week. Beneficial associations have been noted between PBM and bone determinants in older adults (29, 43, 44). Milk intake has shown positive effects on PBM (8, 13, 45, 46), which, if sustained throughout adolescent growth

and into adulthood could favorably modify attainment of bone mass, further delay bone loss, and decrease fracture risk (8, 43, 44, 47, 48). However, relatively few studies have shown a direct association between milk intake in early years and later osteoporotic fracture risk (11, 22, 49). Most studies examining childhood and adolescent milk intake in relation to bone health and later fracture risk rely on recalled data, often times finding inconsistent results.

Milk intake during pregnancy was not associated with risk of hip fracture. During pregnancy a significant transfer of calcium may occur from the bones of the mother to the fetus, thus decreasing the bone mass of the mother (50-52). This theoretically places the mother at an increased risk of osteoporosis and hip fracture later in life, especially if there were no efforts to maintain calcium levels during pregnancy (53, 54). Calcium lost through the noted transfer may be replaced by consuming high levels of calcium through milk and supplements (51, 55). This suspicion has not been verified, and very few studies have been performed to determine the impact of maternal calcium and milk intake on bone changes during pregnancy and as women age. Calcium absorption and excretion during pregnancy are more associated with hormones and changes in calcium homeostasis than with maternal diet (51-53, 55, 56). Results of this study coincide with previous results showing that dietary intake during pregnancy, specifically milk intake, is not related to maternal bone content (54, 55, 57, 58).

Current milk intake was not associated with risk of hip fracture in elderly participants in Utah. Osteoporosis most often presents after a person is fifty years old, and a dramatic rise in the incidence of hip fracture occurs as age increases (59). Bone loss slowly progresses over time, increasing bone vulnerability in older adults (6).

Because of the diagnosis late in life, consideration and prevention of osteoporosis is often postponed. Increasing calcium and other important nutrients, through consumption of low fat milk and dairy products, has been shown in some studies to reduce age-associated bone loss and hip fracture (7, 10, 20, 29, 60-63). Other studies, including this study, have not shown an association between milk consumption and hip fracture for older adults (11, 47, 64-66).

Milk consumption dropped significantly later in life compared to age 18 and during pregnancy among cases, controls, milk drinkers and milk avoiders. Total food intake (6, 9, 35, 67) and milk consumption (29, 43) decreases with age. An especially large decline in milk consumption was seen among milk avoiders, suggesting that milk avoidance may reduce milk consumption later in life.

Also, milk avoiders within both the case and control groups drank significantly less milk than milk drinkers at the age of 18, during pregnancy, and at the time of hip fracture for cases and time of interview for controls. These results are similar to other publications focusing on milk consumption throughout life (11, 60). Milk avoidance for many subjects may be long-term and occur throughout life.

Milk avoiders, among men and women in Utah, with low total calcium intake are at greater risk of hip fracture than non-avoiders, but milk avoiders with high total calcium intake are not at increased risk. Milk avoidance among those with low calcium intake may be detrimental to older adults because of insufficient calcium stores, and decreased bone maintenance, thus increasing the risk of hip fracture. Yet, most of the world's population does not drink milk (31-34). Reasons for milk avoidance are related to lactose intolerance, soft drink preference vs. milk preference, concern about body weight, and

family or personal lifestyle choice (30, 31, 45, 46, 68, 69). Whatever the reason for milk avoidance, these barriers to milk intake have shown an increased fracture risk in both children (30, 45, 68, 70) and in older adulthood (71-74).

At sufficient levels of calcium intake, milk does not seem to aid in hip fracture prevention among this Utah population. Results from the Utah study strengthen previous research showing bone benefit and decreased fracture risk from adequate calcium consumption (23, 24, 35, 54, 75-80). Low milk consumption has been identified as a significant risk factor for hip fracture and high calcium intake in the form of milk was associated with a significantly lower risk of hip fracture among women aged 50 and older (61). A consistent and significant association was found showing that risk of hip fracture decreased as levels of calcium, in both men and women, increased (78). Increasing calcium intake over the life span may augment bone acquisition during growth, stabilize bone mass at maturity, and lessen bone loss during aging (3). Sufficient calcium intake, even among lifetime milk avoiders, may aid in decreasing hip fracture risk.

Several studies are also available showing no association between calcium intake and risk of hip fracture (11, 22, 49, 64, 81-83).

Drinking milk has been strongly and positively associated with calcium intake in this population as well as in other publications (28, 69, 84). About half of all dietary calcium intakes in North America are through milk consumption (47, 68). Most milk avoiders have inadequate calcium intake as seen in previous reports in both children (45, 69) and individuals with lactose intolerance (72, 85). Other nutrients found in significant amounts among milk drinkers compared to milk avoiders in Utah were protein, calories, fat, and vitamin D.

No duration of milk avoidance among this population was found to be more harmful than another. Thus, we cannot predict from the information available that avoiding milk for only one year will increase odds of hip fracture, but we can assume that long-term avoidance leads to this deleterious effect, and only among those with low intakes of total calcium.

This study has possible limitations and biases common to FFQs and case-control studies. An effect of milk intake during specified stages of life may not have been detected secondary to the limitations of the dietary assessment method. Semiquantitive FFQs, including the picture-sort technique, ranks study subjects according to usual nutrient intake. This method is quick, easy to administer and cost-efficient and therefore often used in large population-based studies. Limitations include decreased accuracy and exactness when compared to the food record method or multiple 24-h dietary recall interviews. In this case-control study, self-reported information after the incidence of hip fracture may hold some recall bias and result in altered conclusions. Study participants were nearly all Caucasian and results may differ among other racial or ethnic groups.

In conclusion, milk avoidance was significantly associated with increased risk of osteoporotic hip fracture among elderly men and women in Utah but only among those with low calcium intake. Milk avoiders with low total calcium consumption (Q1, Q2) had increased risk of hip fracture, where milk avoiders with moderate to high total calcium intakes (Q3-Q5) had similar risk of hip fracture compared to non-avoiders. Milk is a good source of calcium and other nutrients related to bone health (20) but increased milk consumption may not be an option for the 75% of the world's population and 30% of the United States population that are lactose intolerant (86). Thus, individuals unable to

drink milk or that choose to avoid this beverage, should obtain adequate calcium from other sources such as fortified cereals and juices, calcium-rich vegetables and supplements.

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Table 1. Characteristics of the Utah Study of Nutrition and Bone Health cohort: 1997 – 2001.[1]

	Female		Male	
	Case (n=854)	Control (n=877)	Case (n=333)	Control (n=447)
Age (y)	76.5 ± 9.0[2]	75.8 ± 9.2	74.9 ± 9.4	73.5 ± 10.5
White race (%)	95.6	98.1	98.5	96.9
Estrogen use (%)				
Never	52.1	43.3[3]	---	---
Former	25.5	25.8	---	---
Current	22.4	30.9	---	---
Smoking (%)				
Never	77.4	83.5[3]	45.0	53.0
Former	15.9	13.8	44.7	39.1
Current	6.7	2.7	10.2	7.8
Regular alcohol use (%)				
Never	72.5	79.5[3]	44.3	49.3
Former	15.2	8.9	32.5	28.0
Current	12.3	11.5	23.2	22.6
Physical Activity (%)				
None	13.3	17.7[4]	16.8	17.2
One	22.9	26.2	29.4	22.1
Two	38.4	33.6	34.2	38.5
Three	25.4	22.5	19.5	22.1
Weight (kg)[6]	63.7 ± 14.2	69.0 ± 14.5[3]	70.0 ± 14.8	82.7 ± 15.2[5]
Height (cm)[6]	162.2 ± 6.7	161.4 ± 6.4[5]	178.9 ± 6.8	176.6 ± 7.5[3]
BMI (kg/M^2)[6]	24.2 ± 5.1	26.5 ± 5.1[3]	25.1 ± 4.1	26.5 ± 4.3[3]
Calcium (mg)[7]	1592 ± 752	1588 ± 776	1346 ± 657	1314 ± 651
Vitamin D (IU)[8]	559 ± 340	545 ± 333	511 ± 303	503 ± 328
Milk intake (cups/wk)				
Age 18	10.3 ± 9.0	10.8 ± 9.1	13.9 ± 11.4	14.6 ± 11.1
Pregnancy[9]	10.3 ± 8.4	11.2 ± 8.6[5]		
Age 50 or older[10]	8.7 ± 8.1[11]	8.8 ± 7.6[11]	8.9 ± 7.8[11]	8.7 ± 8.4[11]
Persons avoiding milk for a year or more (%)				
Yes	15.5	11.1[4]	13.5	10.3
No	84.5	88.9	86.5	89.7
Milk avoidance duration (y)[12]	38.6 ± 29.9	36.6 ± 29.6	23.2 ± 25.1	29.9 ± 28.5

[1] Distribution of covariates of 1,187 cases and 1,324 controls by gender
[2] Mean ± standard deviation (SD)
[3-5]Significant difference between cases and controls within gender, [3]$P \leq 0.001$, [4]$P \leq 0.01$, [5]$P \leq 0.05$
[6] Current weight and height for controls, weight and height at time of hip fracture for cases
[7] Sum of dietary, individual, and multi or combo calcium supplement (mg) per day
[8] Sum of dietary, individual, and multi or combo vitamin D supplement (IU) per day
[9] Includes only women who reported being pregnant. Cases (n= 789), Controls (n= 816)
[10] Current milk intake for controls, milk intake at time of hip fracture for cases
[11] Significant differences between recent milk intake and milk intake at age 18 and during pregnancy, $P \leq 0.001$
[12] Among those reporting at least one year of milk avoidance. Cases (female= 123, male=45), Controls (female= 86, male= 45)

Table 2. Distribution of covariates of 1,187 cases and 1,324 controls by milk avoidance.

	Case		Controls	
	Avoid (n= 177)	Non-avoid (n=1010)	Avoid (n=143)	Non-Avoid (n=1181)
Age, (y)	74.5 ± 9.6[1]	76.4 ± 9.0[2]	74.6 ± 9.3	75.1 ± 9.8
Gender (%)				
Female	74.6	71.5	67.8	66.0
Male	25.4	28.5	32.2	34.0
Estrogen use (%)[5]				
Never	57.8	51.0	44.2	43.2
Former	25.0	25.6	26.3	25.7
Current	17.2	23.4	29.5	31.1
Smoking (%)				
Never	70.1	68.0	65.7	74.1[3]
Former	22.6	24.3	30.8	21.3[3]
Current	7.3	7.7	3.5	4.6
Regular alcohol use (%)				
Never	65.5	64.4	62.7	70.1
Former	22.6	19.6	16.9	15.2
Current	11.9	16.0	20.4	14.7
Physical Activity (%)				
None	14.1	14.4	17.6	17.5
One	26.6	24.5	26.1	24.7
Two	39.0	36.8	33.8	35.4
Three	20.3	24.4	22.5	22.4
Weight (kg)[6]	67.3 ± 17.3	68.5 ± 16.0	72.9 ± 15.7	73.7 ± 16.1
Height (cm)[6]	167.2 ± 10.5	166.8 ± 10.0	166.7± 9.8	166.6 ± 9.9
BMI (kg/M^2)[6]	24.0 ± 5.5	24.5± 4.7	26.2 ± 5.0	26.5 ± 4.8
Calcium (mg)[7]	1233 ± 678	1575 ± 732[4]	1390 ± 802	1508 ± 739
Vitamin D (IU)[8]	405 ± 269	571 ± 335[4]	473 ± 348	537 ± 329[3]
Calories	2123 ± 711	2333 ± 777[4]	2123 ± 702	2212 ± 720
Total Protein (gm)[9]	78.7 ± 29.5	91.8 ± 34.8[4]	80.3 ± 30.3	87.9 ± 32.0[2]
Animal protein (gm)	48.3 ± 22.9	59.7 ± 26.4[4]	49.3 ± 24.1	56.6 ± 24.3[4]
Fat (gm)	86.8 ± 34.6	95.4 ± 37.6[2]	90.1 ± 36.0	89.9 ± 35.6
Milk intake (cups/wk)				
Age 18	8.4 ± 10.5	11.8 ± 9.7[4]	7.2 ± 9.3	12.7 ± 9.9[4]
Pregnancy[10]	6.6 ± 8.9	11.0 ± 8.1[4]	7.1 ± 9.4	11.7± 8.4[4]
Age 50 or older[11]	1.9 ± 4.7[12]	10.0 ± 7.8[4, 12]	2.4 ± 5.5[12]	9.5 ± 7.8[4,12]
Other dairy avoidance (%)[13]				
Yes	19.2	1.2[4]	14.0	1.4[4]
No	80.8	98.8	86.0	98.6

[1]Mean ± standard deviation (SD)
[2-4] Significant difference between cases and controls within gender, [2]$P \leq 0.01$, [3]$P \leq 0.05$, [4]$P \leq 0.001$
[5] Among women
[6] Current weight and height for controls, weight and height at time of hip fracture for cases
[7] Sum of dietary, individual, and multi or combo calcium supplement (mg) per day
[8] Sum of dietary, individual, and multi or combo vitamin D supplement (IU) per day
[9] Sum of protein from both plant and animal sources (gm) per day
[10] Includes only women who reported being pregnant. Cases (n= 789), Controls (n= 816)
[11] Current milk intake for controls, milk intake at time of hip fracture for cases
[12] Significant differences between recent milk intake and milk intake at age 18 and during pregnancy, $P \leq 0.001$
[13] Persons avoiding dairy, other than milk, for a year or more

Table 3. Odds ratio of hip fracture by level of milk intake at age 18.

	Cases	Controls	Odds Ratio (95% Confidence Interval)	
	n	*n*	Crude	Adjusted[1]
0-1 cups/ week	218	209	1.0 (Referent)	1.0 (Referent)
2-7 cups/ week	398	454	0.97 (0.85, 1.09)	0.96 (0.84, 1.10)
8-14 cups/ week	247	257	1.06 (0.91, 1.23)	1.14 (0.97, 1.33)
15+ cups/ week	308	397	0.85 (0.75, 0.98)	0.86 (0.75, 1.00)[2]

[1] Adjusted for gender, age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, total calcium intake and total vitamin D intake.

[2] P = 0.0463, 95% Confidence Intervals (0.745, 0.998)

Table 4. Odds ratio of hip fracture by level of milk intake during pregnancy among women who reported being pregnant.

	Cases	Controls	Odds Ratio (95% Confidence Interval)	
	n	*n*	Crude	Adjusted[1]
0-1 cups/ week	140	128	1.0 (Referent)	1.0 (Referent)
2-7 cups/ week	265	263	1.04 (0.89, 1.22)	1.10 (0.93, 1.31)
8-14 cups/ week	148	172	0.89 (0.70, 1.07)	0.92 (0.76, 1.13)
15+ cups/ week	236	253	0.96 (0.82, 1.13)	0.94 (0.79, 1.12)

[1] Adjusted for age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, total calcium intake and total vitamin D intake.

Table 5. Odds ratio of hip fracture by level of recent milk intake (time of interview for controls, time of hip fracture for cases).

	Cases	Controls	Odds Ratio (95% Confidence Interval)	
	n	*n*	Crude	Adjusted[1]
0-1 cups/ week	269	269	1.0 (Referent)	1.0 (Referent)
2-7 cups/ week	496	588	0.91 (0.81, 1.03)	0.94 (0.83, 1.08)
8-14 cups/ week	263	314	0.90 (0.78, 1.04)	0.90 (0.77, 1.03)
15+ cups/ week	160	153	1.13 (0.94, 1.35)	1.12 (0.91, 1.38)

[1] Adjusted for gender, age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, total calcium intake and total vitamin D intake.

Table 6. Odds ratio of hip fracture associated with milk avoidance.

	Cases	Controls	Odds Ratio (95% Confidence Interval)	
	n	*n*	Crude	Adjusted[1]
Did not avoid milk	1010	1181	1.0 (Referent)	1.0 (Referent)
Avoided milk	177	143	1.45 (1.14, 1.83)	1.38 (1.07, 1.78)[2]

[1] Adjusted for gender, age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, total calcium intake and total vitamin D intake.
[2] P = 0.014

Table 7. Odds ratio of hip fracture by quartile of milk avoidance duration among those who avoided milk for a year or more.

	Cases	Controls	Odds Ratio (95% Confidence Interval)	
	n	*n*	Crude	Adjusted[1]
≤ 6 years	43	38	1.0 (Referent)	1.0 (Referent)
7-25 years	45	31	1.28 (0.68, 2.41)	1.15 (0.57, 2.30)
26-63 years	36	40	0.80 (0.43, 1.49)	0.77 (0.38, 1.54)
≥ 64 years	53	34	1.38 (0.75, 2.54)	1.09 (0.53, 2.24)

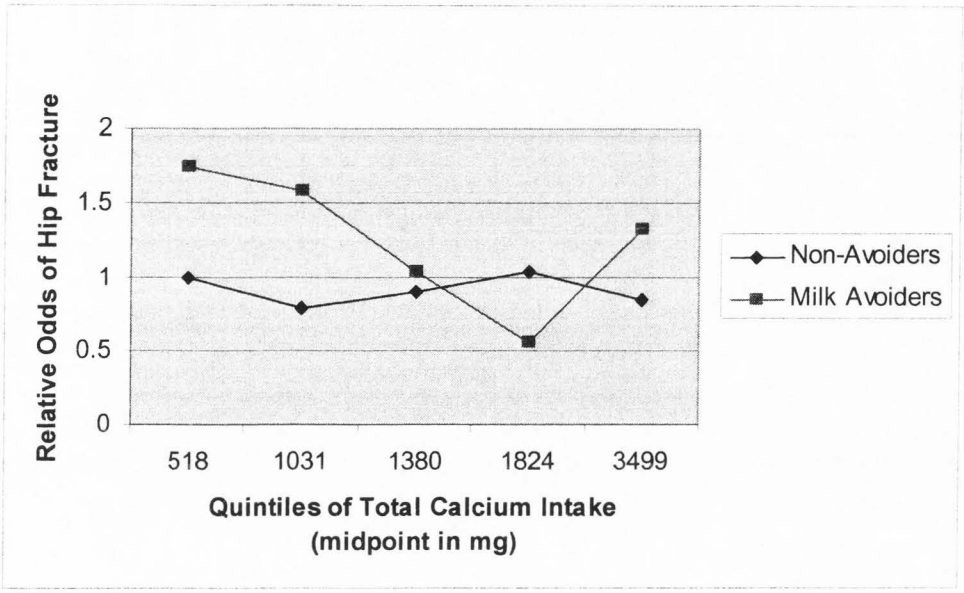
[1] Adjusted for gender, age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, total calcium intake and total vitamin D intake.

Table 8. Odds ratios and 95% confidence intervals of quintiles of calcium by status of milk avoidance and risk of hip fracture.[1]

Calcium Quintiles (mg)	Midpoint	Case		Control		Milk				*P*- value[4]
		n		*n*		Non-Avoiders		Avoiders		
		N-A[2]	A[3]	N-A	A	OR	95% CI	OR	95% CI	
Q1 ($\leq$ 860)	518	171	66	220	43	1.0	Referent	1.72	1.26, 2.17	0.0196
Q2 (861- 1200)	1031	178	39	257	26	0.78	0.48, 1.08	1.58	1.01, 2.15	0.0132
Q3 (1201- 1563)	1380	207	25	243	24	0.89	0.58, 1.20	1.03	0.37, 1.68	0.6693
Q4 (1564- 2085)	1824	227	19	225	30	1.02	0.70, 1.35	0.56	0.00, 1.28	0.0601
Q5 ($\geq$ 2085)	3499	223	26	232	19	0.83	0.47, 1.19	1.32	0.61, 2.04	0.1912

[1] Adjusted for gender, age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, and total vitamin D intake.
[2] Non-Avoiders
[3] Avoiders
[4] P-value of contrasts between milk avoiders and non-avoiders by quintile of calcium intake.

Figure 1. Relative odds of osteoporotic hip fracture by load of total calcium intake and milk avoidance status.[1, 2]



[1] Reference group is milk drinkers (non-avoiders) in the lowest quintile of calcium intake.
[2] Adjusted for gender, age group, estrogen use, body mass index, smoking, alcohol use, regular participation in none, exactly one, exactly two, or all three of yard work, house work, or recreational activities, total calorie intake, total protein intake, and total vitamin D intake.

CHAPTER IV

SUMMARY AND CONCLUSION

Summary

Data from the Utah Study of Nutrition and Bone Health, a statewide case-control study examining men and women aged 50-89 years, were used to investigate milk intake throughout the lifecycle and associated risk of osteoporotic hip fracture. History of milk consumption at age 18, during pregnancy and milk avoidance was obtained through in-person interviews. Milk intake in the one-year period prior to hip fracture for cases and the one-year period prior to interview for controls was assessed using a picture-sort food frequency questionnaire. Logistic regression models were used to assess the association between history of milk intake and risk of hip fracture while controlling for potential confounding factors including physical activity, smoking status, alcohol and estrogen use, age, gender, nutrient intakes, height, weight and body mass index.

Specified life periods including pregnancy and older adulthood portrayed no association between milk intake and risk of hip fracture. Milk intake at age 18 was borderline significant in relation to decreased hip fracture risk and milk intake of 15 or more cups per week. Milk avoidance was found to be significantly associated with increased risk of hip fracture. Further analysis found that only milk avoiders with low total calcium intakes (lowest two quintiles) were at an increased risk of hip fracture, whereas milk avoiders with higher total calcium intakes were not at increased risk. This original research will contribute to the literature on nutrition and bone health.

Further intention of this thesis project was to gain knowledge about epidemiological studies in the field of nutrition, the processes used to examine data, and the topics of hip fracture and associated nutritional factors, specifically milk. A literature review was completed to gain a better understanding of the role of milk in relation to overall individual nutrition throughout the life cycle, bone health and maintenance, calcium balance, peak bone mass, pregnancy, and osteoporosis and hip fracture in older adulthood. Milk avoidance and barriers to regular milk consumption were also reviewed.

Available research on milk intake in association with risk of osteoporotic hip fracture is inconclusive. Milk consumption is beneficial to the nutritional status of persons from childhood until older adulthood. Milk is an efficient and nutrient dense food providing significant amounts of protein, energy, phosphorus, vitamin D, calcium and other beneficial nutrients necessary for bone health. Because of these dietary factors milk may be an important nutrient vehicle in obtaining a high peak bone mass during adolescents and in avoiding undernutrition in elderly individuals. Very few studies are available on maternal milk consumption during pregnancy and most available literature states that dietary intake is not associated with bone health or calcium balance at the time of pregnancy and later in life. Milk avoidance, due to lactose intolerance/ malabsorption, lifestyle choice, taste dislike and soft drink preference verses milk preference, for an extended period of time may cause detrimental effects on bone health and lead to osteoporosis and further hip fracture. The reason for these effects is thought to be inadequate calcium intake among subjects choosing to avoid milk. Milk continues to be recommended for decreasing osteoporosis although current research is still uncertain.

Conclusion

Milk avoiders with low total calcium intake are at a greater risk of hip fracture than non-avoiders, but milk avoiders with higher total calcium intakes are not at greater risk. Most of the world's population does not drink milk for a variety of reasons including lactose intolerance, beverage competition, and personal and family choice. Thus, individuals unable to drink or that choose to avoid milk, should attain adequate calcium from other food sources and supplements in order to prevent increased hip fracture risk.

APPENDICES

APPENDIX A. USNBH INTERVIEW BOOKLET

The Utah Hip Fracture Study
Interview Questionnaire

NIH Grant Number R01-AR43391

Department of Nutrition and Food Sciences
Utah State University
Logan, UT 84322-4450

Revised 8-5-98

START TIME: ☐☐:☐☐ AM or PM

A. INTERVIEW INFORMATION	
A1. DATE OF INTERVIEW:	MONTH:☐☐ DAY:☐☐ YEAR:☐☐☐☐
A2. NAME OF INTERVIEWER:	_____
A3. ID CODE OF INTERVIEWER:	..... ☐☐
A4. SETTING OF INTERVIEW:	HOME OF PARTICIPANT ..... 1 HOME OF FRIEND/RELATIVE ..... 2 HOSPITAL ..... 3 SPECIFY: _____ SKILLED NURSING FACILITY ..... 4 SPECIFY: _____ OTHER INSTITUTION ..... 5 SPECIFY: _____ OTHER ..... 6 SPECIFY: _____
A5. COMPLETE THE INTERVIEW SITE ADDRESS IF DIFFERENT FROM THE FACE SHEET:	_____ STREET ADDRESS _____ CITY _____ STATE _____ ZIP CODE ☐☐☐ - ☐☐☐ - ☐☐☐☐ TELEPHONE

B. DEMOGRAPHICS:
First, I'd like to ask you a few background questions.

B1. In what state were you born?	UTAH ..... 1 OTHER (SPECIFY BELOW) ..... 2 SPECIFY STATE OR COUNTRY: _____ ☐☐
B2. How many years have you lived in Utah?	NUMBER OF YEARS ..... ☐☐
a. Are you a permanent resident of Utah?	YES ..... 1 NO 2
b. How long have you lived in your current residence? (COUNT THE TIME AT RESIDENCE BEFORE HIP FRACTURE FOR CASES.)	NUMBER OF YEARS ..... ☐☐
B3. What best describes your main residence in the (year before your hip fracture/past year)? Was it...	On a farm ..... 1 Rural area, but not a farm or ..... 2 City or town 3
B4. What was your main source of drinking water in the (year before your hip fracture/past year)? Was it a...	City system ..... 1 Rural or county system ..... 2 Private well ..... 3 Bottled water or ..... 4 Something else? (SPECIFY BELOW) ..... 5 _____
B5. During your life, in what city and state have you lived the longest?	CITY_____ ☐☐☐ STATE_____ ☐☐ COUNTRY_____ ☐☐
a. What year did you move there or were you born there?	YEAR ..... ☐☐☐☐
b. What year did you move away?	YEAR ..... ☐☐☐☐ (CODE CURRENT YEAR IF STILL THERE.)

B6. What is your marital status? Are you ...	Married ..... 1 Living with someone as married ..... 2 Separated or divorced ..... 3 Widow/widower ..... 4 Never married ..... 5 RF 7
B7. What is your race or ethnic group?	WHITE, NOT OF HISPANIC ORIGIN ..... 1 AFRICAN AMERICAN ..... 2 ASIAN AMERICAN OR PACIFIC ISLANDER .. 3 (SPECIFIC GROUP:_____) MEXICAN-AMERICAN OR CHICANO ..... 4 PUERTO RICAN, CUBAN, OR OTHER HISPANIC 5 NATIVE AMERICAN OR NATIVE ALASKAN ... 6 (SPECIFIC TRIBE: _____) OTHER OR MIXED ..... 7 (SPECIFIC GROUPS:_____) RF 97
B8. How many years of school did you complete?	1-8 YEARS ..... 1 9-11 YEARS ..... 2 HIGH SCHOOL GRADUATE OR GED ..... 3 VOCATIONAL EDUCATION AFTER HIGH SCHOOL ..... 4 SOME COLLEGE (INCLUDES AA DEGREE) .... 5 COLLEGE GRADUATE (BS, BA) ..... 6 GRADUATE DEGREE (MS, MA, PH.D, MD, JD, DVM) ..... 7 RF 97
B9. What is your religious preference?	CATHOLIC ..... 1 EASTERN ORTHODOX (GREEK OR RUSSIAN) . 2 JEWISH ..... 3 LDS (MORMON) ..... 4 PROTESTANT ..... 5 SEVENTH DAY ADVENTIST ..... 6 OTHER ..... 7 SPECIFY: _____ NO RELIGIOUS PREFERENCE ..... 8 RF 97
B10. About how often did you attend religious services or activities in the (year before your hip fracture/past year)? Would you say ...	Never ..... 1 Less than once a month ..... 2 Once or twice a month ..... 3 Once a week ..... 4 More than once a week ..... 5 RF 7

C. MINI-MENTAL STATE EXAMINATION:
Now, I would like to ask you some questions to check your memory and concentration. Some of the questions may be easy and some will be harder. Take your time if you need to. Just relax and do your best. WRITE DOWN RESPONSES AND CIRCLE RESPONSE CODE AT RIGHT.

C1.	What is the year NOW? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C2.	What is the season of the year? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C3.	What is the month? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C4.	What is the date? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C5.	What is the day of the week? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C6.	What state are we in? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C7.	What county are we in? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C8.	What city or town are we in? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____

C9.	What floor of the building are we on? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C10.	What building are we in? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____

C11. I am going to name three objects. After I have said them, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes. The three objects are: **apple, table, and penny.** Please repeat the names for me now.

SCORE THE FIRST TRY. IF INCORRECT, REPEAT OBJECTS AND ALLOW R TO RECALL FOR UP TO THREE TRIALS ONLY.

	OBJECT	CORRECT	ERROR	RF	NOT ASSESSED
a.	APPLE	 1	 2	 7	 8
b.	TABLE	 1	 2	 7	 8
c.	PENNY	 1	 2	 7	 8
d.	HOW MANY TRIALS WERE NEEDED?			NUMBER OF TRIALS ..... ☐	

C12. Now I am going to give you a word and ask you to spell it forwards and backwards. The word is "world." First, will you spell "world" forwards for me?

REPEAT OR HELP R SPELL WORLD FORWARDS, IF NECESSARY.

Now spell the word "world" backwards.

WRITE LETTERS EXACTLY AS R RECITES THEM TO YOU.
SCORE 1 POINT FOR EACH LETTER IN CORRECT BACKWARD ORDER, BEFORE THE FIRST MISTAKE.
ENTER SCORE IN OPEN BOX (MAXIMUM = 5)

RECORD LETTERS HERE AS GIVEN:

__ __ __ __ __
(forwards)

__ __ __ __ __ ..... ☐
(backwards)
NOT ASSESSED (EXPLAIN) 8
_____

C13. What were the three objects I asked you to remember? (SCORE RECALL ONLY. OBJECTS DO NOT HAVE TO BE IN ORDER)

	CORRECT	ERROR	RF	NOT ASSESSED
a. APPLE	1	2	7	8
b. TABLE	1	2	7	8
c. PENNY	1	2	7	8

C14.	POINT TO YOUR WATCH What is this called? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C15.	SHOW YOUR PENCIL What is this called? _____	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C16.	I would like you to repeat a phrase after me. The phrase is, "No ifs, ands, or buts." Please repeat it to me now. SCORE FIRST RESPONSE, MAY REPEAT INSTRUCTIONS UP TO TWO TIMES.	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____
C17.	HOLD UP THE SHEET WITH "CLOSE YOUR EYES" STATEMENT IN FRONT OF R. Please read the words on this page and then do exactly what it says. CODE CORRECT IF R CLOSES EYES.	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____

C18. I am going to give you a piece of paper. When I do, take the paper in your right hand, fold the paper in half with both hands, and place it on your lap.

READ THE FULL STATEMENT THEN HAND OVER THE "CLOSE YOUR EYES" PAPER. DO NOT REPEAT INSTRUCTIONS OR COACH. SCORE EACH PART BELOW.

		CORRECT	ERROR	RF	NOT ASSESSED
a.	RIGHT HAND	 1	 2	 7	 8
b.	FOLDS	 1	 2	 7	 8
c.	ON LAP	 1	 2	 7	 8

C19. Please write any complete sentence on that piece of paper for me.	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____ ☐☐
C20. Here is a drawing. Please copy the drawing on the same paper exactly as it appears.	CORRECT ..... 1 ERROR ..... 2 RF ..... 7 NOT ASSESSED (EXPLAIN) ..... 8 _____ ☐☐

D. ACTIVITIES OF DAILY LIVING AND PHYSICAL ACTIVITY Now, I'd like to ask you about activities that we often do as part of our daily lives. I would like to know if during the (month before your hip fracture/past month) you needed help with these activities, or if you could do them without any help.	
D1. Did you need help with eating, for example, serving your food, using utensils, or drinking from a glass or cup?	YES ..... 1 NO 2
D2. Did you need help preparing meals for yourself, for example making a hot meal, a sandwich, or a TV dinner or microwaving food?	YES ..... 1 NO 2
D3. Did you need help bathing, including running the water, washing any part of your body, washing your hair, getting in or out of the tub or shower?	YES ..... 1 NO 2
D4. Did you need help using the toilet, including adjusting clothing, cleaning yourself, getting onto or off of the toilet, or reminders to use the toilet?	YES ..... 1 NO 2
D5. Did you need help dressing yourself, including getting out of clothes, putting clothes on, fastening clothes together, or putting on shoes?	YES ..... 1 NO 2
D6. Did you need help getting into or out of bed or a chair?	YES ..... 1 NO 2
D7. Did you use a cane, walker, or some other form of assistance to help you walk?	YES ..... 1 NO 2
D8. Could you walk short distances by yourself within your own home or inside a building? This would include assistance with a cane or walker.	YES ..... 1 NO 2
D9. Could you walk longer distances by yourself, that is a block or more? This would include assistance with a cane or walker.	YES ..... 1 NO 2
D10. Were you able to climb 10 or more stairs without help?	YES ..... 1 NO 2
D11. Did you need help doing light housework such as dusting, washing dishes, sweeping, or doing laundry?	YES ..... 1 NO 2
D12. Did you need any kind of help using the telephone, either answering the phone or placing calls? This would include use of an amplifier or larger push button numbers.	YES ..... 1 NO 2
D13. Did you need help with shopping for groceries or prescriptions?	YES ..... 1 NO 2
D14. Did you need help or reminders to take your medications, other than a pill box?	YES ..... 1 NO 2

D15. Did you need anyone to help with managing your finances, such as paying the bills or balancing your checkbook?	YES ..... 1 NO 2
D16. Could you drive a car by yourself?	YES ..... 1 NO 2
D17. Did you receive home delivered meals such as Meals on Wheels?	YES ..... 1 NO 2
D18. Did you attend a senior center?	YES ..... 1 NO 2
D19. Did you eat lunch at a center or participate in a congregate meal service?	YES ..... 1 NO 2
D20. Did you feel that you had enough contacts with other people?	YES ..... 1 NO 2

E. WEIGHT AND HEIGHT HISTORY: The next series of questions is about your weight and height.		
E1.	CASES: What was your weight at the time of your hip fracture? CONTROLS: What is your current weight?	..... POUNDS ☐☐☐
E2.	CASES: What was your height at the time of your hip fracture? CONTROLS: What is your current height?	..... FEET ☐ ..... INCHES ☐☐
E3.	**What was your weight at age 18, around the time that you may have finished high school?**	..... POUNDS ☐☐☐
E4.	**What was your height at age 18?**	..... FEET ☐ ..... INCHES ☐☐
E5.	**What was the most you ever weighed? OTHER THAN WHEN PREGNANT.** a. **How old were you at your maximum weight?**	..... POUNDS ☐☐☐ AGE IN YEARS ..... ☐☐☐
E6.	Have you ever lost more than 20 pounds in one year or less for any reason? OTHER THAN FOLLOWING A PREGNANCY. a. What was the most weight that you have ever lost at one time? b. Was that weight loss a result of your dieting?	YES ..... 1 NO (SKIP TO SECTION F) ..... 2 ..... POUNDS ☐☐☐ YES ..... 1 NO (SKIP TO E8) ..... 2 DK (SKIP TO E8) 8
E7.	At times that you lost 20 pounds or more, what types of diets did you use?	_____ ☐☐ _____ ☐☐ _____ ☐☐

E8.	Was your weight loss of 20 pounds or more ever a result of increased physical activity, work, or exercise?	YES (SPECIFY ACTIVITIES BELOW) ..... 1 NO ..... 2 DK ..... 8 TYPE OF ACTIVITIES: _____ ☐☐ _____ ☐☐ _____ ☐☐

E9. Was your weight loss of 20 pounds or more ever a result of ...

a.	... surgery?	YES ..... 1 NO 2
b.	... feeling blue, sad or depressed?	YES ..... 1 NO 2
c.	... illness?	YES (SPECIFY ILLNESS BELOW) ..... 1 NO ..... 2 TYPE OF ILLNESS: _____ ☐☐ _____ ☐☐

F. PHYSICAL ACTIVITY: The next questions are related to physical activity.	
F1. In the (year before your hip fracture/past year), how many hours each day did you sit while watching TV, a VCR, reading, or while doing other seated activities? Would you say it was ...	Less than 5 hours per day, or ... 1 Between 5-10 hours per day, or . 2 More than 10 hours per day 3
F2. In the (year before your hip fracture/ past year) did you ever go for walks? This would include times that you walked for exercise, to visit, shop or while hiking, fishing, hunting, or golfing.	YES ..... 1 NO (SKIP TO F3) 2
a. How often did you take walks?	NUMBER OF WALKS ..... ☐☐ PER { DAY ..... 1 WEEK ..... 2 MONTH 3
b. How long did you walk each time, on average?	MINUTES ..... ☐☐☐
c. How far did you walk each time, on average? (8 CITY BLOCKS = 1 MILE)	MILES ..... ☐☐.☐☐

I'd now like to ask you about several kinds of active work or recreation you may have done at any time in your adult life, meaning since the age of 18. Since the age of 18 did you ever regularly...

	ACTIVITY	(IF NO SKIP TO NEXT ACTIVITY) YES	NO	a. Did you do (ACTIVITY) in the (year before your hip fracture/past year)? (IF NO GO TO C) YES	NO	b. During that year, how much time did you spend doing (ACTIVITY) per day, week, month or year? (GO TO NEXT ACTIVITY) MIN. D W M Y	c. At what age did you stop doing (ACTIVITY)? AGE
F3.	... do heavy housework including vacuuming, mopping, scrubbing floors or sidewalks, moving furniture or boxes?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F4.	... ever do garden or yard work including digging, weeding, cutting grass, raking, or snow shoveling?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F5.	... ever jog or run?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F6.	... ever use an exercise bike, treadmill, or other exercise machine?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F7.	... ever ride a bicycle outside?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years

	Since the age of 18, did you ever regularly... ACTIVITY	(IF NO SKIP TO NEXT ACTIVITY) YES	NO	a. Did you do (ACTIVITY) in the (year before your hip fracture/past year)? (IF NO GO TO C) YES	NO	b. During that year, how much time did you spend doing (ACTIVITY) per day, week, month or year? (GO TO NEXT ACTIVITY) MIN. D W M Y	c. At what age did you stop doing (ACTIVITY)? AGE
F8.	... swim laps?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F9.	... ever do aerobics classes or aerobic dance?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F10.	... ever do other kinds of dancing including square dancing, country western swing dance, ballroom dancing or other kinds?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F11.	... ever do calisthenics or other similar exercises?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F12.	... ever do yoga, Tai-chi exercise, or other similar exercise?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F13.	... ever ski downhill or cross-country ski?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F14.	... ever play tennis, racquet ball, or squash?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years
F15.	... ever lift weights?	1	2	1	2	☐☐☐ D W M Y	☐☐☐ years

G. OCCUPATIONAL HISTORY

The next group of questions is about work you have had during your life time.

G1. What kind of work have you done for the majority of your working life, for example, homemaker, farmer, rancher, electrical engineer, typist, sales clerk?	_____ KIND OF WORK ☐☐☐☐☐☐☐☐
a. How old were you when you started doing this type of work?	AGE IN YEARS ..... ☐☐
b. How many years did you do this type of work?	NUMBER OF YEARS ..... ☐☐ (IF HOMEMAKER, SKIP TO G1e)
c. What was the name of the company or business?	_____ ☐☐☐☐ NAME OF COMPANY OR BUSINESS
d. What kind of business or industry was this (for example, TV and radio manufacturing, retail store or work at home or on a farm)?	_____ ☐☐☐☐ KIND OF BUSINESS
e. What were your most frequent activities or duties (for example, typing, keeping account books, selling cars, keeping house)?	1._____ _____ ☐☐☐☐ 2._____ _____ ☐☐☐☐ 3._____ _____ ☐☐☐☐
f. I'd like to know about the activity level of this job. Did you ... RESPONSE 3: WOULD CAUSE A SLIGHT INCREASE IN HEART RATE AND LIGHT PERSPIRATION. RESPONSE 4: WOULD CAUSE A SUBSTANTIAL INCREASE IN HEART RATE AND HEAVY PERSPIRATION	Usually sit with only minimal standing and walking, or ..... 1 Stand or walk most of your working time, or ..... 2 Carry loads less than ten pounds or walk continuously most of your working hours, or ..... 3 Carry loads of ten pounds or more, walk briskly, climb or dig most of your working hours 4

G2. Has there been another kind of work you have done for 5 or more years? (NOT NECESSARILY CONSECUTIVE YEARS)	YES ..... 1 NO (SKIP TO G4) 2
a. What kind of work was that?	_____ KIND OF WORK ☐☐☐☐☐☐☐☐
b. How old were you when you started doing this type of work?	AGE IN YEARS ..... ☐☐
c. How many years did you do this type of work?	NUMBER OF YEARS ..... ☐☐ (IF HOMEMAKER, SKIP TO G2f)
d. What was the name of the company or business?	_____ ☐☐☐☐ NAME OF COMPANY OR BUSINESS
e. What kind of business or industry was this (for example, TV and radio manufacturing, retail store or work at home or on a farm)?	_____ ☐☐☐☐ KIND OF BUSINESS
f. What were your most frequent activities or duties (for example, typing, keeping account books, selling cars, keeping house)?	1._____ _____ ☐☐☐☐ 2._____ _____ ☐☐☐☐ 3._____ _____ ☐☐☐☐
g. I'd like to know about the activity level of this job. Did you ... RESPONSE 3: WOULD CAUSE A SLIGHT INCREASE IN HEART RATE AND LIGHT PERSPIRATION. RESPONSE 4: WOULD CAUSE A SUBSTANTIAL INCREASE IN HEART RATE AND HEAVY PERSPIRATION	Usually sit with only minimal standing and walking, or ..... 1 Stand or walk most of your working time, or ..... 2 Carry loads less than ten pounds or walk continuously most of your working hours, or ..... 3 Carry loads of ten pounds or more, walk briskly, climb or dig most of your working hours 4

G3. Has there been another kind of work you have done for 5 or more years?	YES ..... 1 NO (SKIP TO G4) 2
a. What kind of work was that?	_____ KIND OF WORK ☐☐☐☐☐☐☐☐
b. How old were you when you started doing this type of work?	AGE IN YEARS ..... ☐☐
c. How many years did you do this type of work?	NUMBER OF YEARS ..... ☐☐ (IF HOMEMAKER, SKIP TO G3f)
d. What was the <u>name</u> of the company or business?	_____ ☐☐☐ NAME OF COMPANY OR BUSINESS
e. What <u>kind</u> of business or industry was this (for example, TV and radio manufacturing, retail store or work at home or on a farm)?	_____ ☐☐☐ KIND OF BUSINESS
f. What were your most frequent activities or duties (for example, typing, keeping account books, selling cars, keeping house)?	1._____ _____ ☐☐☐ 2._____ _____ ☐☐☐ 3._____ _____ ☐☐☐
g. I'd like to know about the activity level of this job. Did you ... <u>RESPONSE 3</u>: WOULD CAUSE A SLIGHT INCREASE IN HEART RATE AND LIGHT PERSPIRATION. <u>RESPONSE 4</u>: WOULD CAUSE A SUBSTANTIAL INCREASE IN HEART RATE AND HEAVY PERSPIRATION	Usually sit with only minimal standing and walking, or ..... 1 Stand or walk most of your working time, or ..... 2 Carry loads less than ten pounds or walk continuously most of your working hours, or ..... 3 Carry loads of ten pounds or more, walk briskly, climb or dig most of your working hours 4
G4. What was your employment status (at the time of your hip fracture/during the last month)? Were you...	Employed ..... 1 Retired ..... 2 A homemaker ..... 3 Able to work but unemployed ..... 4 Disabled and unable to work ..... 5 Or something else ..... 6 SPECIFY: _____ ☐☐

H. NUTRITIONAL ASSESSMENT
The next part of the interview is an activity that will help us find out about your diet.

H1.	ADMINISTER PICSORT FOOD FREQUENCY QUESTIONNAIRE	
H2.	What kind of oil, fat or shortening do you usually cook with? (MARK 1 CHOICE.)	OIL (LIST MAIN TYPE) ..... 1 TYPE OF OIL: _____ SOFT OR TUB MARGARINE ..... 2 STICK MARGARINE ..... 3 BUTTER ..... 4 LARD, FATBACK, BACON FAT ..... 5 VEGETABLE SHORTENING ..... 6 PAM OR NO OIL ..... 7 DON'T COOK ..... 8 DK 98
H3.	What kind of oil, fat or shortening do you usually add to vegetables, potatoes, and breads or rolls? (MARK 1 CHOICE.)	OIL (LIST MAIN TYPE) ..... 1 TYPE OF OIL: _____ SOFT OR TUB MARGARINE ..... 2 STICK MARGARINE ..... 3 BUTTER ..... 4 LARD, FATBACK, BACON FAT ..... 5 PAM OR NO OIL ..... 6 DON'T ADD FAT ..... 7 DK 98
H4.	Thinking back to your younger years, how often per week did you drink an 8 ounce glass of milk when you were 18 years old, or around the time you may have finished high school?	GLASSES PER WEEK ..... ☐☐
H5.	Please tell me if you have ever avoided any of the following foods in your diet, for any reason, for a year or more. Have you ever avoided ...	
a.	... all red meat, that is beef, pork, and lamb?	YES (SPECIFY NUMBER OF YEARS) . 1 NO ..... 2 NUMBER OF YEARS ..... ☐☐
b.	... chicken and turkey?	YES (SPECIFY NUMBER OF YEARS) . 1 NO ..... 2 NUMBER OF YEARS ..... ☐☐
c.	... fish?	YES (SPECIFY NUMBER OF YEARS) . 1 NO ..... 2 NUMBER OF YEARS ..... ☐☐

d. ... eggs?	YES (SPECIFY NUMBER OF YEARS) . 1 NO . . . . . 2 NUMBER OF YEARS . . . . . ☐☐
e. ... milk?	YES (SPECIFY NUMBER OF YEARS) . 1 NO . . . . . 2 NUMBER OF YEARS . . . . . ☐☐
f. ... other dairy products, that is cheese, yogurt and ice cream?	YES (SPECIFY NUMBER OF YEARS) . 1 NO . . . . . 2 NUMBER OF YEARS . . . . . ☐☐

J. DIETARY SUPPLEMENTS:
Now, I would like to ask you about your use of dietary supplements in the (year before your hip fracture/past year). Would you please take out any bottles of vitamins, minerals, or other dietary supplements that you have taken.

J1. Did you regularly take multi vitamin/mineral supplements in the (year before your hip fracture/past year)?	YES ..... 1 NO (SKIP TO J2) 2
a. What specific brand or brands of multivitamin/minerals do you use? ASK FOR THE BOTTLES AND RECORD FULL NAME OF BRAND AND TYPE.	BRAND AND TYPE: _____ ☐☐☐☐ _____ ☐☐☐☐ _____ ☐☐☐☐
b. How many years have you taken multivitamin/minerals?	NUMBER OF YEARS ..... ☐☐
c. How often did you take them?	NUMBER OF TIMES ..... ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8
J2. Other than a multivitamin/mineral, did you regularly take any combination of two or more vitamins or minerals that came in a single pill in the (year before your hip fracture/past year)?	YES ..... 1 NO (SKIP TO J5) 2
a. What specific brand and type of combination dietary supplement do you use? ASK FOR THE BOTTLES AND RECORD FULL NAME OR BRAND AND TYPE.	BRAND AND TYPE: _____ ☐☐☐☐ _____ ☐☐☐☐
b. How many years have you taken this combination dietary supplement?	NUMBER OF YEARS ..... ☐☐
c. How often did you take them?	NUMBER OF TIMES ..... ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8

J3. Did you regularly take any other combination dietary supplement in the (year before your hip fracture/past year)?	YES ..... 1 NO (SKIP TO J5) 2
a. What specific brand and type of combination dietary supplement do you use? ASK FOR THE BOTTLES AND RECORD FULL NAME OR BRAND AND TYPE.	BRAND AND TYPE: _____ ☐☐☐☐ _____ ☐☐☐☐
b. How many years have you taken this combination dietary supplement?	NUMBER OF YEARS ..... ☐☐
c. How often did you take them?	NUMBER OF TIMES ..... ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8
J4. Did you regularly take any other combination dietary supplement in the (year before your hip fracture/past year)?	YES ..... 1 NO (SKIP TO J5) 2
a. What specific brand and type of combination dietary supplement do you use? ASK FOR THE BOTTLES AND RECORD FULL NAME OR BRAND AND TYPE.	BRAND AND TYPE: _____ ☐☐☐☐ _____ ☐☐☐☐
b. How many years have you taken this combination dietary supplement?	NUMBER OF YEARS ..... ☐☐
c. How often did you take them?	NUMBER OF TIMES ..... ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8

Now, I am going to ask you about individual vitamins, minerals, and other dietary supplements that you take by themselves. I would also like to know the strength or dose of the dietary supplement and how often you took them. You don't need to tell me again about the vitamins, minerals, and other dietary supplements we've already recorded.

a. In the (year before your hip fracture/past year) did you regularly take... IF NO SKIP TO NEXT VITAMIN	b. How many years have you taken (VITAMIN)?	c. How often did you take them?	d. What dose did you usually take each time?
J5. YES ..... 1 NO ..... 2 Vitamin A	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN IU .. ☐☐☐☐☐ Less THAN 8000 IU ..... 1 8,000 TO 13, 000 IU ..... 2 13,001 TO 22,000 IU ..... 3 22,001 IU OR MORE ..... 4 DK 8
J6. YES ..... 1 NO ..... 2 Beta carotene	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN IU .. ☐☐☐☐☐ LESS THAN 5,000 IU ..... 1 5,000 TO 10,000 IU ..... 2 10,001 TO 25,000 IU ..... 3 25,001 IU OR MORE ..... 4 DK 8
J7. YES ..... 1 NO ..... 2 Vitamin C	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG . ☐☐☐☐☐ LESS THAN 400 MG ..... 1 400 TO 700 MG ..... 2 701 TO 1300 MG ..... 3 1301 MG OR MORE ..... 4 DK 8
J8. YES ..... 1 NO ..... 2 Vitamin E	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN IU .. ☐☐☐☐☐ LESS THAN 100 IU ..... 1 100 TO 500 IU ..... 2 501 TO 1000 IU ..... 3 1001 IU OR MORE ..... 4 DK 8

a. In the (year before your hip fracture/past year) did you regularly take... IF NO SKIP TO NEXT VITAMIN	b. How many years have you taken (VITAMIN)?	c. How often did you take them?	d. What dose did you usually take each time?
J9. YES ..... 1 NO ..... 2 Calcium	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG . ☐☐☐☐ LESS THAN 400 MG ..... 1 400 TO 900 MG ..... 2 901 TO 1300 MG ..... 3 1301 MG OR MORE ..... 4 DK 8
J10. YES ..... 1 NO ..... 2 Vitamin D	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN IU .. ☐☐☐☐ LESS THAN 200 IU ..... 1 200 TO 400 IU ..... 2 401 TO 1,000 IU ..... 3 1,001 IU OR MORE ..... 4 DK 8
J11. YES ..... 1 NO ..... 2 Vitamin B6	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG ... ☐☐☐ LESS THAN 10 MG ..... 1 10 TO 50 MG ..... 2 51 TO 100 MG ..... 3 101 MG OR MORE ..... 4 DK 8
J12. YES ..... 1 NO ..... 2 Vitamin B12	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE MCG .... ☐☐☐ LESS THAN 20 MCG ..... 1 20 TO 100 MCG ..... 2 101 TO 250 MCG ..... 3 251 MCG OR MORE ..... 4 DK 8
J13. YES ..... 1 NO ..... 2 Niacin	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG ... ☐☐☐ LESS THAN 20 MG ..... 1 20 MG TO 50 MG ..... 2 51 TO 100 MG ..... 3 101 MG OR MORE ..... 4 DK 8

a. In the (year before you hip fracture/past year) did you regularly take... IF NO SKIP TO NEXT VITAMIN	b. How many years have you taken (VITAMIN)?	c. How often did you take them?	d. What dose did you usually take each time?
J14. YES ..... 1 NO ..... 2 Folic Acid	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE MCG . ☐☐☐☐ LESS THAN 300 MCG .... 1 300 TO 400 MCG ..... 2 401 TO 800 MCG ..... 3 801 MCG OR MORE ..... 4 DK 8
J15. YES ..... 1 NO ..... 2 Selenium	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE MCG .... ☐☐☐☐ LESS THAN 80 MCG ..... 1 80 TO 130 MCG ..... 2 131 TO 250 MCG ..... 3 251 MCG OR MORE ..... 4 DK 8
J16. YES ..... 1 NO ..... 2 Iron	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG ..... ☐☐☐ LESS THAN 25 MG ..... 1 25 TO 75 MG ..... 2 76 TO 100 MG ..... 3 101 MG OR MORE ..... 4 DK 8
J17. YES ..... 1 NO ..... 2 Magnesium	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG ... ☐☐☐☐ LESS THAN 200 MG ..... 1 200 TO 300 MG ..... 2 301 TO 400 MG ..... 3 401 MG OR MORE ..... 4 DK 8
J18. YES ..... 1 NO ..... 2 Zinc	NUMBER OF YEARS .. ☐☐.☐	NUMBER OF TIMES ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8	DOSE IN MG ... ☐☐☐☐ LESS THAN 25 MG ..... 1 25 TO 75 MG ..... 2 76 TO 100 MG ..... 3 101 MG OR MORE ..... 4 DK 8

J19.	In the (year before your hip fracture/past year) did you regularly take herbal preparations?	YES ..... 1 NO (SKIP TO J20) 2
	a. What specific brand and type of herbal preparation do you use? ASK FOR THE BOTTLES AND RECORD FULL NAME OR BRAND AND TYPE.	BRAND AND TYPE: _____ ☐☐☐☐ _____ ☐☐☐☐ _____ ☐☐☐☐
	b. How many years did you take herbal preparations?	NUMBER OF YEARS ..... ☐☐.☐
	c. How often did you take them?	NUMBER OF TIMES ..... ☐☐ PER{ DAY ..... 1 WEEK ..... 2 MONTH ..... 3 YEAR ..... 4 DK 8
J20.	In the (year before your hip fracture/past year) did you regularly take...	
	a. Any other nutritional supplement?	YES (SPECIFY BELOW) ..... 1 NO ..... 2 BRAND AND TYPE: _____ ☐☐☐☐ _____ ☐☐☐☐ _____ ☐☐☐☐

K. MEDICATION HISTORY:
Now I would like to ask you about medications you have taken.

K1.	During the (year before your hip fracture/past year), have you taken any medications that were prescribed for you or were prescribed for someone else and given to you by family members or friends?	YES ..... 1 NO ..... 2 RF ..... 7 DK 8
K2.	We are also interested in other medications that do not require a prescription, such as aspirin, other pain killers, laxatives, cold medicines, or herbal medicines. During the (year before your hip fracture/past year), have you taken any non-prescription medications?	YES ..... 1 NO ..... 2 RF ..... 7 DK 8
	INTERVIEW CHECKPOINT: IS K1 OR K2 = Yes?	YES (CONTINUE) ..... 1 NO (SKIP TO K6) 2
K3.	May I please see all the prescription and non-prescription medication (containers) that you used in the (year before your hip fracture/past year)? LET R GATHER MEDICATIONS. Let's put them into two separate piles.	
	SEPARATE THE PRESCRIPTION FROM THE NON-PRESCRIPTION DRUGS. LIST ALL PRESCRIPTION MEDICATIONS ACROSS ROW A ON THE MEDICATION INVENTORY.	
K4.	Are there any other prescription medications you've used in the (year before your hip fracture/past year) that you don't have here?	
	LIST ANY ADDITIONAL PRESCRIPTION MEDICATIONS ACROSS ROW A ON THE MEDICATION INVENTORY. RECORD OR ASK B-H FOR ALL PRESCRIPTION MEDICATIONS LISTED.	

K5.	Now I would also like to ask you about the non-prescription medications that you have taken in the (year before your hip fracture/past year). First, let me list the non-prescription medications you have here.	
	LIST ALL NON-PRESCRIPTION MEDICATIONS PROVIDED ON THE MEDICATION INVENTORY.	
K5a.	Are there any other non-prescription medications that you've taken in the (year before your hip fracture/past year) that you don't have a bottle for?	
	LIST ANY ADDITIONAL NON-PRESCRIPTION MEDICATIONS ACROSS ROW A AND RECORD OR ASK B-H FOR ALL NON-PRESCRIPTION MEDICATIONS.	
K6.	I would like you to think very carefully over your past and try to remember if you have ever been bothered by any of these illnesses or problems...	
a.	...headaches or migraine headaches?	YES ..... 1 NO 2
b.	... joint pain or back pain, including arthritis, gout, bursitis, rheumatism, or other joint pain?	YES ..... 1 NO 2
c.	...pain from injuries or operations, or other medical procedures or chronic conditions?	YES ..... 1 NO 2
	INTERVIEWER CHECKPOINT: IF SUBJECT ANSWERED NO TO ALL CONDITIONS IN K6, SKIP TO K9.	
	SHOW DRUG CARD I	
K7.	Please look at this card. It is a list of medications that are often taken for the painful or inflammatory conditions that we just discussed. Can you read the names of the drugs without difficulty?	YES (ALLOW SUBJECT TO LOOK AT LIST) . 1 NO (READ ALOUD TO SUBJECT) 2

K8.	You don't have to tell me again about your medications that we already recorded. Could you please tell me if, in the (year before your hip fracture/past year), you have ever used any of the medications on this card regularly?	YES ..... 1 NO (SKIP TO K9) 2
	AS EACH MEDICATION IS REPORTED BY RESPONDENT, RECORD ON MEDICATION INVENTORY AND ASK QUESTIONS B-H FOR EACH MEDICATION.	
	IF RESPONDENT CAN NOT READ, CONTINUE TO READ ENTIRE LIST UNTIL R REPORTS ALL USAGE FOR DRUGS ON THIS CARD.	
K9.	Now I would like to ask you about some stomach, bowel or gastrointestinal problems. Have you ever had a problem with...	
a.	...ulcers, heartburn or indigestion?	YES ..... 1 NO 2
b.	...gastritis, esophagitis, reflux or hiatal hernia?	YES ..... 1 NO 2
c.	...irritable bowel syndrome, constipation, diarrhea or other stomach or bowel problems?	YES ..... 1 NO 2
	INTERVIEWER CHECKPOINT: IF SUBJECT ANSWERED NO TO ALL CONDITIONS IN K9, GO TO K11.	

	SHOW DRUG CARD II	
K10.	Remember, you don't have to tell me about the medications we have already recorded. After we have read this list, could you please tell me if, in the (year before your hip fracture/past year), you have ever used any of the medications on this card regularly for any of the stomach, bowel, or digestive conditions we just talked about?	YES ..... 1 NO 2
	AS EACH MEDICATION IS REPORTED BY RESPONDENT, RECORD ON MEDICATION INVENTORY AND ASK QUESTIONS B-H FOR EACH MEDICATION.	
K11.	Have you ever had problems with...	
a.	...hay fever, seasonal allergies or asthma?	YES ..... 1 NO 2
b.	...chronic colds, bronchitis, sinus problems or pneumonia?	YES ..... 1 NO 2
c.	Have you had emphysema or chronic obstructive pulmonary disease?	YES ..... 1 NO 2
	INTERVIEWER CHECKPOINT: IF SUBJECT ANSWERED NO TO ALL CONDITIONS IN K11 GO TO K13.	
	SHOW DRUG CARD III	
K12.	Here is another drug card. Remember, you don't have to tell me again about the medications we have already recorded. After we have read this list, could you please tell me if, in the (year before your hip fracture/past year), you have ever used any of the medicines on this card regularly?	YES ..... 1 NO 2
	AS EACH MEDICATION IS REPORTED BY RESPONDENT, RECORD ON MEDICATION INVENTORY AND ASK QUESTIONS B-H FOR EACH MEDICATION.	

K13.	Now, I would like to ask about problems people often have with sleep, their nerves, or their mood. Have you ever ...	
a.	... had sleep problems, anxiety or nerve problems?	YES ..... 1 NO 2
b.	... been sad, felt blue, down or depressed for two weeks or more?	YES ..... 1 NO 2
c.	...had manic-depression, bipolar disorder, schizophrenia or other mental health problems?	YES ..... 1 NO 2
d.	...had seizures or convulsions?	YES ..... 1 NO 2

IF NO TO ALL CONDITIONS IN K13, SKIP TO SECTION L.

SHOW DRUG CARD IV

K14.	Here is another drug card. After we have read this list, could you please tell me if, in the (year before your hip fracture/past year), you have ever used any of the medications on this card regularly?	YES ..... 1 NO 2

AS EACH MEDICATION IS REPORTED BY RESPONDENT, RECORD ON MEDICATION INVENTORY AND ASK QUESTIONS B-H FOR EACH MEDICATION.

L. MEDICAL HISTORY:

L1. Has a doctor ever told you that you had osteoporosis or bone loss? Osteoporosis includes broken bones due to bone loss and thinning of bones that occurs with aging, loss of height because of bone loss in the spine, or a "Dowager's hump" in the spine because of bone loss.	YES ..... 1 NO (SKIP TO L2) ..... 2 DK (SKIP TO L2) 8
a. How old were you when you were told that you had osteoporosis?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for osteoporosis?	YES ..... 1 NO (SKIP TO L2) ..... 2 DK 8
c. Are there any medications that you have taken for osteoporosis (in the year before your hip fracture/past year) that you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L2. Has a doctor ever told you that you had arthritis?	**YES ..... 1** **NO (SKIP TO L3) ..... 2** **DK (SKIP TO L3) 8**
a. What type of arthritis did you have? Was it...	**Osteoarthritis ..... 1** **Rheumatoid arthritis ..... 2** **Both osteoarthritis and rheumatoid arthritis ..... 3** **Other (SPECIFY BELOW) ..... 4** _____ ☐☐☐ **DK 8**
b. Did you have arthritis in your hip joint(s)?	YES ..... 1 NO ..... 2 DK 8
c. Did you have arthritis in your knee(s)?	YES ..... 1 NO ..... 2 DK 8
d. Did you have arthritis in your feet?	YES ..... 1 NO ..... 2 DK 8
d. Did you have arthritis in your hand(s)?	YES ..... 1 NO ..... 2 DK 8

e. Did you have arthritis in your elbow(s)?	YES ..... 1 NO ..... 2 DK 8
f. Did you have arthritis in your shoulder(s)?	YES ..... 1 NO ..... 2 DK 8
g. Did you have arthritis in your spine or back?	YES ..... 1 NO ..... 2 DK 8
h. How old were you when you were first told that you had arthritis?	AGE IN YEARS ..... ⌊⌊⌊⌋
i. Did you receive medical treatment or medication for your arthritis?	YES ..... 1 NO (SKIP TO L3) ..... 2 DK 8
j. Are there any medications that you have taken for arthritis (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L3. Has a doctor ever told you that you had high blood pressure or hypertension?	YES ..... 1 NO (SKIP TO L4) ..... 2 DK (SKIP TO L4) 8
a. How old were you when you were told that you had high blood pressure or hypertension?	AGE IN YEARS ..... ⌊⌊⌋
b. Did you receive medical treatment or medication for high blood pressure or hypertension?	YES ..... 1 NO (SKIP TO L4) ..... 2 DK 8
c. Are there any medications that you have taken for high blood pressure (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L4. Has a doctor ever told you that you had a heart attack?	YES ..... 1 NO (SKIP TO L5) ..... 2 DK (SKIP TO L5) 8
a. How old were you when you were told that you had a heart attack?	AGE IN YEARS ..... ⌊⌊⌋
b. Did you receive medical treatment or medication for your heart attack?	YES ..... 1 NO (SKIP TO L5) ..... 2 DK 8
c. Are there any medications you have taken for your heart attack (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2

L5. Has a doctor ever told you that you had a stroke?	YES ..... 1 NO (SKIP TO L6) ..... 2 DK (SKIP TO L6) 8
a. How old were you when you were told that you had a stroke?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for your stroke?	YES ..... 1 NO (SKIP TO L6) ..... 2 DK 8
c. Are there any medications you have taken for your stroke (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L6. Has a doctor ever told you that you had diabetes?	YES ..... 1 NO (SKIP TO L7) ..... 2 DK (SKIP TO L7) 8
a. How old were you when you were told that you had diabetes?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for your diabetes?	YES ..... 1 NO (SKIP TO L7) ..... 2 DK 8
c. Are there any medications you have taken for your diabetes (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2

L7. Has a doctor ever told you that you had cancer?	YES . . . . . 1 NO (SKIP TO L8) . . . . . 2 DK (SKIP TO L8) 8
a. What type of cancer was it (PRIMARY SITE)?	_____ ☐☐☐
b. How old were you when you were told that you had this type of cancer?	AGE IN YEARS . . . . . ☐☐☐
c. Did you receive medical treatment for this type of cancer?	YES . . . . . 1 NO 2
d. Did you have another type of cancer?	YES . . . . . 1 NO (SKIP TO L7I) 2
e. What type of cancer was it (PRIMARY SITE)?	_____ ☐☐☐
f. How old were you when you were told that you had this type of cancer?	AGE IN YEARS . . . . . ☐☐☐
g. Did you receive medical treatment for this type of cancer?	YES . . . . . 1 NO 2
h. Did you have another type of cancer?	YES . . . . . 1 NO (SKIP TO L7I) 2
i. What type of cancer was it (PRIMARY SITE)?	_____ ☐☐☐
j. How old were you when you were told that you had this type of cancer?	AGE IN YEARS . . . . . ☐☐☐
k. Did you receive medical treatment for this type of cancer?	YES . . . . . 1 NO 2
l. Are there any medications you have taken for your cancer (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) . . . . . 1 NO 2
L8. Has a doctor ever told you that you had kidney disease?	YES . . . . . 1 NO (SKIP TO L9) . . . . . 2 DK (SKIP TO L9) 8
a. How old were you when you were told that you had kidney disease?	AGE IN YEARS . . . . . ☐☐☐
b. Did you receive medical treatment or medication for your kidney disease?	YES . . . . . 1 NO (SKIP TO L9) . . . . . 2 DK 8
c. Are there any medications you have taken for your kidney disease (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) . . . . . 1 NO 2

L9. (WOMEN ONLY) Has a doctor ever told you that you had endometriosis?	YES ..... 1 NO (SKIP TO L10) ..... 2 DK (SKIP TO L10) 8
a. How old were you when you were told that you had endometriosis?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for your endometriosis?	YES ..... 1 NO (SKIP TO L10) ..... 2 DK 8
c. Are there any medications you have taken for your endometriosis (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L10. Has a doctor ever told you that you needed "blood thinners?"	YES ..... 1 NO (SKIP TO L11) ..... 2 DK (SKIP TO L11) 8
a. How old were you when you were told that you needed "blood thinners?"	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication to thin your blood?	YES ..... 1 NO (SKIP TO L11) ..... 2 DK 8
c. Are there any medications you have taken to thin your blood (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L11. Has a doctor ever told you that you had thyroid disease or goiter?	YES ..... 1 NO (SKIP TO L12) ..... 2 DK (SKIP TO L12) 8
a. How old were you when you were told that you had thyroid disease or goiter?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for your thyroid disease or goiter?	YES ..... 1 NO (SKIP TO L12) ..... 2 DK 8
c. Are there any medications you have taken for your thyroid disease or goiter (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2

L12. Has a doctor ever told you that you had parathyroid disease?	YES ..... 1 NO (SKIP TO L13) ..... 2 DK (SKIP TO L13) 8
a. How old were you when you were told that you had parathyroid disease?	AGE IN YEARS ..... ⌊⌊⌊⌋
b. Did you receive medical treatment or medication for your parathyroid disease?	YES ..... 1 NO (SKIP TO L13) ..... 2 DK 8
c. Are there any medications you have taken for your parathyroid disease (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L13. Has a doctor ever told you that you had cataracts?	YES ..... 1 NO (SKIP TO L14) ..... 2 DK (SKIP TO L14) 8
a. How old were you when you were told that you had cataracts?	AGE IN YEARS ..... ⌊⌊⌊⌋
b. Did you receive medical treatment or medication for your cataracts?	YES ..... 1 NO (SKIP TO L14) ..... 2 DK 8
c. Are there any medications you have taken for your cataracts (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L14. Has a doctor ever told you that you had glaucoma?	YES ..... 1 NO (SKIP TO L15) ..... 2 DK (SKIP TO L15) 8
a. How old were you when you were told that you had glaucoma?	AGE IN YEARS ..... ⌊⌊⌊⌋
b. Did you receive medical treatment or medication for your glaucoma?	YES ..... 1 NO (SKIP TO L15) ..... 2 DK 8
c. Are there any medications you have taken for your glaucoma (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2

L15. Has a doctor ever told you that you had memory loss?	YES ..... 1 NO (SKIP TO L16) ..... 2 DK (SKIP TO L16) 8
a. How old were you when you were told that you had memory loss?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for your memory loss?	YES ..... 1 NO (SKIP TO L16) ..... 2 DK 8
c. Are there any medications you have taken for your memory loss (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L16. Has a doctor ever told you that you had Parkinson's disease?	YES ..... 1 NO (SKIP TO L17) ..... 2 DK (SKIP TO L17) 8
a. How old were you when you were told that you had Parkinson's disease?	AGE IN YEARS ..... ☐☐☐
b. Did you receive medical treatment or medication for your Parkinson's disease?	YES ..... 1 NO (SKIP TO L17) ..... 2 DK 8
c. Are there any medications you have taken for your memory loss (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
L17. Has a doctor ever told you that you had multiple sclerosis?	YES ..... 1 NO (SKIP TO SECTION M) ..... 2 DK (SKIP TO SECTION M) 8
a. How old were you when you were told that you had multiple sclerosis?	AGE IN YEARS ..... ☐☐☐
b. Did you receive treatment for your multiple sclerosis?	YES ..... 1 NO (SKIP TO SECTION M) ..... 2 DK 8
c. Are there any medications you have taken for your multiple sclerosis (in the year before your hip fracture/past year) you have not told me about?	YES (GO TO MI) ..... 1 NO 2
RECORD ADDITIONAL MEDICATIONS TAKEN IN THE (YEAR BEFORE HIP FRACTURE/PAST YEAR) ON THE MEDICATION INVENTORY AND ASK QUESTIONS B-H FOR EACH ADDITIONAL MEDICATION.	

M. HISTORY OF BONE FRACTURES:
Now I'd like to ask you some questions about your personal history of bone fractures.

M1.	Have you ever broken your hip? This includes your hip joint or the top of your femur or thigh bone, near your hip.	YES ..... 1 NO (SKIP TO M7) ..... 2 DK (SKIP TO M7) 8
M2.	Which side of your hip did you fracture?	LEFT ..... 1 RIGHT ..... 2 BOTH ..... 3 DK 8
M3.	What was the date of your most recent hip fracture?	MONTH:☐☐ DAY:☐☐ YEAR:☐☐☐☐
M4.	I'd like to ask you some questions about your hip fracture.	
	a. Did it happen because of a fall?	YES (SKIP TO M5) ..... 1 NO 2
	b. How did you fracture your hip, if other than a fall?	_____ ☐☐ _____ ☐☐ _____ ☐☐ (SKIP TO M6)
M5.	Now I'd like to ask you some questions about your fall.	
	a. What were you doing at the time of the fall? Were you...	Lying still ..... 1 Sitting still ..... 2 Standing still ..... 3 Transferring or changing position ..... 4 Walking on a level surface ..... 5 Stepping up or down ..... 6 Running or other vigorous activity .... 7 Other (SPECIFY BELOW) ..... 8 _____ ☐☐ DK 98

b. How far did you fall? Was it...	From bed to the floor ..... 1 From a seated position ..... 2 From a standing position ..... 3 A standing fall from the height of one step or curb ..... 4 A standing fall from the height of two steps ..... 5 A standing fall from the height of a chair or stool ..... 6 A standing fall from a height greater than a chair or stool ..... 7 Other (SPECIFY INCLUDING HEIGHT) ... 8 _____ ☐☐ DK 98
c. What type of surface did you hit when you fell? Was it ...	A thick, padded rug or carpet ..... 1 A rug without padding ..... 2 A bare wood floor ..... 3 Linoleum or soft tile ..... 4 Ceramic (hard) tile ..... 5 Concrete, cement, or asphalt ..... 6 Dirt, grass, or soft snow ..... 7 Hard ice or packed snow ..... 8 Other (SPECIFY BELOW) ..... 9 _____ ☐☐ DK 98
d. What direction did you fall? Was it... CIRCLE ONE RESPONSE. IF SIDEWAYS, PROBE FOR RIGHT OR LEFT AND CIRCLE APPROPRIATE CODE. USE CODE 2 ONLY IF SIDEWAYS AND R DOES NOT KNOW IF THEY FELL TO THE RIGHT OR LEFT.	Forward ..... 1 Sideways (DK RIGHT OR LEFT) ..... 2 To the right ..... 3 To the left ..... 4 Backward ..... 5 Other (SPECIFY BELOW) ..... 6 _____ ☐☐ DK 8
e. Just before the fall did you feel dizzy or weak?	YES ..... 1 NO ..... 2 DK 8
f. Just before the fall did you feel faint or lose consciousness?	YES ..... 1 NO ..... 2 DK 8
g. Just before the fall was your vision impaired for any reason?	YES (SPECIFY BELOW) ..... 1 _____ ☐☐ NO ..... 2 DK 8

h.	Just before the fall did you trip on an object?	YES (SPECIFY BELOW) .... 1 ________________ ☐☐ NO .... 2 DK 8
M6.	Did you fracture your hip another time before your last fracture?	YES .... 1 NO (SKIP TO M7) 2
a.	Please tell me the date of each earlier time that you broke your hip.	.... MONTH:☐☐ YEAR:☐☐☐☐ .... MONTH:☐☐ YEAR:☐☐☐☐
M7.	I'd like to ask you about other bones that you may have broken. Have you broken any other bones <u>since you were 18 years old</u>?	YES .... 1 NO (SKIP TO SECTION N) 2
M8.	Please tell me the dates of fractures, the bones fractured, and how the fracture occurred. Let's start with the most recent time that you broke one or more bones.	

What was the date of your fracture(s)?	**Which bones were fractured?**	**How did the fracture(s) occur?**
MONTH:☐☐ YEAR:☐☐☐☐	________ ☐☐☐ ________ ☐☐☐ ________ ☐☐☐	________ ________ ________ ☐☐☐
MONTH:☐☐ YEAR:☐☐☐☐	________ ☐☐☐ ________ ☐☐☐ ________ ☐☐☐	________ ________ ________ ☐☐☐
MONTH:☐☐ YEAR:☐☐☐☐	________ ☐☐☐ ________ ☐☐☐ ________ ☐☐☐	________ ________ ________ ☐☐☐
MONTH:☐☐ YEAR:☐☐☐☐	________ ☐☐☐ ________ ☐☐☐ ________ ☐☐☐	________ ________ ________ ☐☐☐

N. FAMILY HISTORY OF BONE FRACTURE AND BONE DISEASE:

I would like to ask you about your blood relatives and whether or not any of them have ever had a hip fracture or other problems with their bones known as osteoporosis.

Osteoporosis includes broken bones due to bone loss and thinning of bones that occurs with aging, loss of height because of bone loss in the spine, or a "Dowager's hump" in the spine because of bone loss.

N1. First, did your own biological mother ever have a hip fracture?	YES ..... 1 NO (SKIP TO N2) ..... 2 DK (SKIP TO N2) 8
a. What was your mother's age at the time of her first hip fracture?	AGE IN YEARS ..... ☐☐☐
b. How did the fracture occur?	_____ ☐☐ _____ ☐☐
N2. Did a doctor ever tell your mother that she had osteoporosis?	YES ..... 1 NO (SKIP TO N3) ..... 2 DK (SKIP TO N3) 8
a. At what age was your mother told that she had some problems due to osteoporosis?	AGE IN YEARS ..... ☐☐☐
N3. Did your biological father ever have a hip fracture?	YES ..... 1 NO (SKIP TO N4) ..... 2 DK (SKIP TO N4) 8
a. What was your father's age at the time of his first hip fracture?	AGE IN YEARS ..... ☐☐☐
b. How did the hip fracture occur?	_____ ☐☐ _____ ☐☐
N4. Did a doctor ever tell your father that he had osteoporosis?	YES ..... 1 NO (SKIP TO N5) ..... 2 DK (SKIP TO N5) 8
a. At what age was your father told that he had some problems due to osteoporosis?	AGE IN YEARS ..... ☐☐☐
N5. How many daughters do you have?	NUMBER OF DAUGHTERS ..... ☐☐ (IF NONE, ENTER 00 AND SKIP TO N8)

N6. Have any of your daughters had a hip fracture?	YES ..... 1 NO (SKIP TO N7) ..... 2 DK (SKIP TO N7) 8
a. How many of your daughters had a hip fracture?	NUMBER OF DAUGHTERS WITH HIP FRACTURE ..... ☐☐
N7. Did a doctor ever tell (any of) your daughter(s) that she had osteoporosis?	YES ..... 1 NO (SKIP TO N8) ..... 2 DK (SKIP TO N8) 8
a. How many of your daughters had this condition?	NUMBER OF DAUGHTERS WITH THIS CONDITION ..... ☐☐
N8. How many sons do you have?	NUMBER OF SONS ..... ☐☐ (IF NONE, ENTER 00 AND SKIP TO N11)
N9. Have any of your sons had a hip fracture?	YES ..... 1 NO (SKIP TO N10) ..... 2 DK (SKIP TO N10) 8
a. How many of your sons had a hip fracture?	NUMBER OF SONS WITH HIP FRACTURE ..... ☐☐
N10. Did a doctor ever tell (any of) your son(s) that he had osteoporosis?	YES ..... 1 NO (SKIP TO N11) ..... 2 DK (SKIP TO N11) 8
a. How many of your sons had this condition?	NUMBER OF SONS WITH THIS CONDITION ..... ☐☐
I would now like to ask you the same questions about your brothers and sisters. I will first ask you about your full brothers, that is, those brothers who have the same parents as you.	
N11. How many full-brothers do you have?	NUMBER OF FULL-BROTHERS ..... ☐☐ (IF NONE, ENTER 00 AND SKIP TO N14)
N12. Have any of your full-brothers had a hip fracture?	YES ..... 1 NO (SKIP TO N13) ..... 2 DK (SKIP TO N13) 8
a. How many of your full-brothers had a hip fracture?	NUMBER OF FULL-BROTHERS WITH A HIP FRACTURE ..... ☐☐
N13. Did a doctor ever tell (any of) your full-brother(s) that he had osteoporosis?	YES ..... 1 NO (SKIP TO N14) ..... 2 DK (SKIP TO N14) 8
a. How many of your full-brothers had this condition?	NUMBER OF FULL-BROTHERS WITH THIS CONDITION ..... ☐☐

I would now like to ask you about your half-brothers, that is, those brothers who have only the same mother or only the same father as you.	
N14. How many half-brothers do you have?	NUMBER OF HALF-BROTHERS ..... ☐☐ (IF NONE, ENTER 00 AND SKIP TO N17)
N15. Have any of your half-brothers had a hip fracture?	YES ..... 1 NO (SKIP TO N16) ..... 2 DK (SKIP TO N16) 8
a. How many of your half-brothers had a hip fracture?	NUMBER OF HALF-BROTHERS WITH A HIP FRACTURE ..... ☐☐
N16. Did a doctor ever tell (any of) your half-brother(s) that he had osteoporosis?	YES ..... 1 NO (SKIP TO N17) ..... 2 DK (SKIP TO N17) 8
a. How many of your half-brothers had this condition?	NUMBER OF HALF-BROTHERS WITH THIS CONDITION ..... ☐☐
N17. How many full-sisters do you have?	NUMBER OF FULL-SISTERS ..... ☐☐ (IF NONE, ENTER 00 AND SKIP TO N20)
N18. Have any of your full-sisters had a hip fracture?	YES ..... 1 NO (SKIP TO N19) ..... 2 DK (SKIP TO N19) 8
a. How many of your full-sisters had a hip fracture?	NUMBER OF FULL-SISTERS WITH A HIP FRACTURE ..... ☐☐
N19. Did a doctor ever tell (any of) your full-sister(s) that she had osteoporosis?	YES ..... 1 NO (SKIP TO N20) ..... 2 DK (SKIP TO N20) 8
a. How many of your full-sisters had this condition?	NUMBER OF FULL-SISTERS WITH THIS CONDITION ..... ☐☐
N20. How many half-sisters do you have?	NUMBER OF HALF-SISTERS ..... ☐☐ (IF NONE, ENTER 00 AND SKIP TO SECTION P)
N21. Have any of your half-sisters had a hip fracture?	YES ..... 1 NO (SKIP TO N22) ..... 2 DK (SKIP TO N22) 8
a. How many of your half-sisters had a hip fracture?	NUMBER OF HALF-SISTERS WITH A HIP FRACTURE ..... ☐☐

N22. Did a doctor ever tell (any of) your half-sister(s) that she had osteoporosis?	YES ..... 1 NO (SKIP TO SECTION P) ..... 2 DK (SKIP TO SECTION P) 8
a. How many of your half-sisters had this condition?	NUMBER OF HALF-SISTERS WITH THIS CONDITION ..... ☐☐

P. PERSONAL HISTORY OF FALLS:		
P1.	In the (year before your hip fracture/past year), have you fallen? (FOR CASES, EXCLUDE FALL THAT CAUSED HIP FRACTURE, IF APPLICABLE)	YES ..... 1 NO (SKIP TO SECTION Q) 2
P2.	How many times in the (year before your hip fracture/past year), have you fallen?	NUMBER OF FALLS ..... ☐☐☐
P3.	What were the main reasons for your falls?	_____ ☐☐☐ _____ ☐☐☐ _____ ☐☐☐

INTERVIEWER CHECK POINT:	IF RESPONDENT IS FEMALE →CONTINUE ..... 1 IF RESPONDENT IS MALE → SKIP TO SECTION S 2

Q. REPRODUCTIVE HISTORY (WOMEN ONLY)

Now I would like to ask some questions about your menstrual history and pregnancies.

Q1.	Have you ever been pregnant? I would like to know about all of your pregnancies, even if the pregnancy did not result in the birth of a live baby.	YES ..... 1 NO (SKIP TO SECTION R) ..... 2 DK (SKIP TO SECTION R) 8
Q2.	Including all live births, stillbirths, miscarriages, and abortions, how many times have you been pregnant?	NUMBER OF PREGNANCIES ..... ☐☐
Q3.	How many live births did you have?	NUMBER OF LIVE BIRTHS ..... ☐☐ (IF NONE CODE 00 AND SKIP TO Q6)
Q4.	How many children did you breast feed?	NUMBER OF CHILDREN BREAST FED ..... ☐☐ (IF NONE CODE 00 AND SKIP TO Q6)
Q5.	How many months did you (usually) breast feed your child (children)?	NUMBER OF MONTHS ..... ☐☐
Q6.	How old were you when you first became pregnant?	AGE IN YEARS ..... ☐☐☐
Q7.	How old were you when you were last pregnant?	AGE IN YEARS ..... ☐☐☐
Q8.	How often per week did you drink a cup of milk during your pregnancies?	NUMBER OF TIMES PER WEEK ..... ☐☐

R. MENOPAUSE AND ESTROGEN USE (WOMEN ONLY)

Now I would like to ask questions about menopause and hormone or estrogen use.

R1.	Have you gone through your menopause or change of life? (That is, have your menstrual periods stopped completely for at least one year?)	YES ..... 1 NO (SKIP TO R2) ..... 2 DK (SKIP TO R2) 8
a.	How old were you when your menstrual periods stopped completely?	AGE IN YEARS ..... ⌊⌊⌋⌋
b.	What was the reason that your menstrual periods stopped completely? Was it due to ...	Natural menopause; "change of life" ..... 1 A hysterectomy (uterus and/or ovaries were removed in surgery) ..... 2 Taking medication that stopped periods ... 3 Or something else? (SPECIFY) ..... 4 SPECIFY:_____
R2.	**Has your uterus (womb) been surgically removed?**	**YES** ..... 1 **NO (SKIP TO R3)** ..... 2 **DK (SKIP TO R3)** 8
a.	**How old were you when your uterus was surgically removed?**	AGE IN YEARS ..... ⌊⌊⌋⌋
R3.	**Have your ovaries been surgically removed?**	**YES (ONE OVARY)** ..... 1 **YES (BOTH OVARIES)** ..... 2 **NO (SKIP TO R4)** ..... 3 **DK (SKIP TO R4)** 8
a.	How old were you when your last ovary was removed?	AGE IN YEARS ..... ⌊⌊⌋⌋
R4.	Have you ever taken estrogen pills or tablets, also called female hormone pills, other than for contraception?	YES ..... 1 NO (SKIP TO R5) ..... 2 DK (SKIP TO R5) 8
a.	How old were you when you first started taking estrogen pills?	AGE IN YEARS ..... ⌊⌊⌋⌋
b.	Are you still taking estrogen pills?	YES (SKIP TO R5) ..... 1 NO 2
c.	How old were you when you stopped taking estrogen pills?	AGE IN YEARS ..... ⌊⌊⌋⌋

R5. Did your doctor ever prescribe a progesterone pill, such as Provera, either alone or to go along with your estrogen prescription?	YES (SPECIFY, IF KNOWN) ..... 1 _____ ☐☐ NO (SKIP TO R6) 2
a. How many days a month did you take this pill?	DAYS PER MONTH ..... ☐☐
R6. Have you ever used estrogen in a patch on your skin such as Estraderm?	YES ..... 1 NO (SKIP TO R7) 2
a. How old were you when you started using the estrogen patch?	AGE IN YEARS ..... ☐☐☐
b. Are you still using the estrogen patch?	YES (SKIP TO R7) ..... 1 NO 2
c. How old were you when you stopped using the estrogen patch?	AGE IN YEARS ..... ☐☐☐
R7. Have you ever used any type of estrogen cream such as Premarin cream or Estrace cream?	YES ..... 1 NO (SKIP TO R8) 2
a. How old were you when you started using the estrogen cream?	AGE IN YEARS ..... ☐☐☐
b. Are you still using the estrogen cream?	YES (SKIP TO R8) ..... 1 NO 2
c. How old were you when you stopped using the estrogen cream?	AGE IN YEARS ..... ☐☐☐
R8. Have you ever used any other form of estrogen (other than for contraception) including herbal products, such as wild yam cream?	YES ..... 1 NO (SKIP TO R9) 2
a. What kind(s) of estrogen did you use?	SPECIFY: _____ ☐☐☐ SPECIFY: _____ ☐☐☐
b. How old were you when you started using (medication listed in R8a)?	AGE IN YEARS ..... ☐☐☐
c. Are you still using (medication listed in R8a)?	YES ..... 1 NO (SKIP TO R9) 2
d. How old were you when you stopped using (name of medication listed in R8a)?	AGE IN YEARS ..... ☐☐☐

R9. Have you ever taken oral contraceptives or birth control pills for any reason?	YES ..... 1 NO (SKIP TO SECTION S) 2
a. How old were you when you first started taking oral contraceptives or birth control pills?	AGE IN YEARS ..... ⌊_⌊_⌊_
b. How old were you when you stopped taking oral contraceptives or birth control pills?	AGE IN YEARS ..... ⌊_⌊_⌊_

S. SMOKING/TOBACCO HISTORY:
The next few questions are about the use of tobacco.

S1.	In your lifetime, have you ever smoked cigarettes, cigars, a pipe, chewed tobacco, or dipped snuff?	YES ..... 1 NO (SKIP TO SECTION T) ..... 2 RF (SKIP TO SECTION T) ..... 7 DK (SKIP TO SECTION T) 8
S2.	Have you ever smoked 100 cigarettes or more in your lifetime?	YES ..... 1 NO (SKIP TO S3) ..... 2 RF (SKIP TO S3) ..... 7 DK (SKIP TO S3) 8
	a. How old were you when you started to smoke cigarettes regularly?	AGE IN YEARS ..... ☐☐☐
	b. Do you smoke cigarettes now?	YES (SKIP TO d) ..... 1 NO ..... 2 RF 7
	c. How old were you when you last smoked cigarettes regularly?	AGE IN YEARS ..... ☐☐☐
	d. How many cigarettes (do/did) you usually smoke per day? 20 CIGARETTES = 1 PACK	CIGARETTES PER DAY ..... ☐☐☐
S3.	Was there ever a time when you smoked cigars once a week or more?	YES ..... 1 NO (SKIP TO S4) ..... 2 RF (SKIP TO S4) ..... 7 DK (SKIP TO S4) 8
	a. How old were you when you started to smoke cigars regularly?	AGE IN YEARS ..... ☐☐☐
	b. Do you smoke cigars now?	YES (SKIP TO d) ..... 1 NO ..... 2 RF 7
	c. How old were you when you last smoked cigars regularly?	AGE IN YEARS ..... ☐☐☐
	d. How many cigars (do/did) you usually smoke per week?	CIGARS PER WEEK ..... ☐☐☐

S4. Was there ever a time when you smoked a pipe once a week or more?	YES ..... 1 NO (SKIP TO S5) ..... 2 RF (SKIP TO S5) ..... 7 DK (SKIP TO S5) 8
a. How old were you when you started to smoke a pipe regularly?	AGE IN YEARS ..... ☐☐☐
b. Do you smoke a pipe now?	YES (SKIP TO d) ..... 1 NO ..... 2 RF 7
c. How old were you when you last smoked a pipe regularly?	AGE IN YEARS ..... ☐☐☐
d. How many pipefuls (do/did) you usually smoke per day?	PIPEFULS PER DAY ..... ☐☐☐
S5. Was there ever a time when you chewed tobacco or dipped snuff once a week or more?	YES ..... 1 NO (SKIP TO SECTION T) ..... 2 RF (SKIP TO SECTION T) ..... 7 DK (SKIP TO SECTION T) 8
a. How old were you when you started to chew tobacco or dip snuff regularly?	AGE IN YEARS ..... ☐☐☐
b. Do you chew tobacco or dip snuff now?	YES (SKIP TO d) ..... 1 NO ..... 2 RF 7
c. How old were you when you last chewed tobacco or dipped snuff regularly?	AGE IN YEARS ..... ☐☐☐
d. How many chews or dips of tobacco/snuff (do/did) you usually chew per day?	CHEWS/DIPS PER DAY ..... ☐☐☐

T. USE OF ALCOHOL:

The next few questions are about the use of alcoholic beverages, like beer, wine, or liquor that people drink at meals, special occasions, or when just relaxing.

T1.	Have you ever had a can or glass of beer, a glass of wine, or a shot of liquor or a mixed drink during your lifetime?	YES ..... 1 NO (SKIP TO SECTION U) ..... 2 RF (SKIP TO SECTION U) ..... 7 DK (SKIP TO SECTION U) 8
T2.	Have you ever regularly drank one or more of these alcoholic beverages a month?	YES ..... 1 NO (SKIP TO T3) ..... 2 RF (SKIP TO T3) ..... 7 DK (SKIP TO T3) 8
	a. At what age did you begin?	AGE IN YEARS ..... ☐☐☐
	b. Did you drink alcohol in the (year before your hip fracture/past year)?	YES ..... 1 NO (SKIP TO T3) ..... 2 RF (SKIP TO T3) ..... 7 DK (SKIP TO T3) 8
	c. How often did you drink alcohol per week?	TIMES PER WEEK ..... ☐☐
	d. When you drank, how many drinks would you have each time?	DRINKS EACH TIME ..... ☐☐

1 DRINK = 1 CAN OR 12 OZ BEER, 1 GLASS OR 4 OZ WINE, OR 1 SHOT OF HARD LIQUOR OR A MIXED DRINK.

T3.	From time to time, people may have occasion to drink more than usual. Have there been any days when you drank 12 or more drinks in one 24-hour period? (Twelve drinks is about one pint of liquor, or two bottles of wine, or two six-packs of beer.)	YES ..... 1 NO (SKIP TO SECTION U) ..... 2 RF (SKIP TO SECTION U) ..... 7 DK (SKIP TO SECTION U) 8
	a. How many times in the (year before your hip fracture/past year) did you drink this amount?	NUMBER OF TIMES ..... ☐☐
	b. Thinking back over your life, how many times did you drink this much alcohol in one day?	1-3 ..... 1 4-10 ..... 2 11 OR MORE 3

U. CONTACTS, FOLLOW-UP INFORMATION, AND CLOSING OF INTERVIEW

U1. In the future, it may become necessary to contact you for additional information. We may need to gather more information on your health or on other topics important to our study. In the event that we cannot reach you, is there a relative or close friend, who does not live with you, who will always know where to contact you?

YES 1
NO 2
RESPONDENT REFUSED TO GIVE FUTURE CONTACT 7

U2a.	U2b.
First name	First name
Last name	Last name
Relationship to participant	Relationship to participant
Street Address	Street Address
City, State	City, State
Zip Code	Zip Code
___-___-____ Telephone number	___-___-____ Telephone number

U3. Please tell me your Social Security Number. This is important for helping us to contact you again. This will be kept confidential like the rest of the information from this interview.

___-__-____
RF 7
DK 8

U4. **FOR CONTROLS ONLY.** READ THE FFQ FOLLOW-UP STUDY CONSENT FORM TO THE RESPONDENT.

DID R AGREE TO PARTICIPATE IN FFQ FOLLOW-UP STUDY?

YES 1
NO 2

U5. TIME INTERVIEW WAS COMPLETED: ___:___ AM PM (CIRCLE ONE)

U6. COMPLETE PHLEBOTOMY

U7. CLOSING STATEMENT AND "THANK YOU" TO PARTICIPANT

U8. INTERVIEWER ASSESSMENT OF QUALITY OF INTERVIEW

GOOD 1
FAIR 2
UNSATISFACTORY 3

V. ADDITIONAL INTERVIEWER OBSERVATION:		
V1.	COULD THE RESPONDENT HEAR YOU CLEARLY?	YES ..... 1 HAD SOME DIFFICULTY BUT COULD COMPLETE INTERVIEW ..... 2 NO 3
V2.	WAS THE RESPONDENT'S SPEECH CLEAR?	YES ..... 1 HAD SOME DIFFICULTY BUT COULD COMPLETE INTERVIEW ..... 2 NO 3
V3.	WAS THE RESPONDENT WELL-ORIENTED TO TIME AND PLACE?	YES ..... 1 SOMEWHAT CONFUSED BUT COULD COMPLETE INTERVIEW ..... 2 NO, VERY DISORIENTED 3
V4.	WAS THE RESPONDENT'S VISION GOOD ENOUGHT TO READ THE MEDICATION CARDS AND TO SEE THE FOOD PICTURES?	YES ..... 1 HAD SOME DIFFICULTY BUT COULD COMPLETE INTERVIEW ..... 2 NO 3
V5.	WAS THERE ANYTHING UNUSUAL ABOUT THIS INTERVIEW THAT YOU WOULD LIKE TO DESCRIBE?	_____ _____ _____ _____ _____

APPENDIX B. THE UTAH PICTURE-SORT FOOD FREQUENCY QUESTIONAIRE

RESPONDENT ID: ⌊⌊⌊⌊⌋-⌊⌊⌊⌊⌋

BEVERAGES

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Plain water from a tap or bottled	001	⌊⌊	D W M Y N
Milk (SPECIFY TYPE BELOW)	002	⌊⌊	D W M Y N
What type of milk do you drink most often?	SKIM/NO FAT ..... 1 LOW FAT (1-2%) ..... 2 WHOLE ..... 3 BUTTERMILK 4		
Ensure or other supplemental beverages (SPECIFY TYPE)	003	⌊⌊	D W M Y N
What types and brands of supplemental beverages do you drink most often?	_____ ⌊⌊⌊ _____ ⌊⌊⌊ _____ ⌊⌊⌊		
Chocolate milk or hot cocoa	005	⌊⌊	D W M Y N
Orange juice	006	⌊⌊	D W M Y N
Other fruit juices	007	⌊⌊	D W M Y N
Diet cola with caffeine	008	⌊⌊	D W M Y N
Coke, Pepsi and other regular colas	009	⌊⌊	D W M Y N
Coffee, regular	010	⌊⌊	D W M Y N
Hot tea or iced tea	011	⌊⌊	D W M Y N
Beer	012	⌊⌊	D W M Y N
Red wine	013	⌊⌊	D W M Y N
White wine	014	⌊⌊	D W M Y N
Liquor, whiskey, gin, mixed drinks	015	⌊⌊	D W M Y N

FRUITS

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Orange	016	⌊⌊	D W M Y N
Grapefruit	017	⌊⌊	D W M Y N
Banana	018	⌊⌊	D W M Y N
Cantaloupe	019	⌊⌊	D W M Y N
Prunes	020	⌊⌊	D W M Y N
Apple or pear	021	⌊⌊	D W M Y N
Applesauce	022	⌊⌊	D W M Y N
Peach, apricot, plum, nectarine	023	⌊⌊	D W M Y N
Watermelon	024	⌊⌊	D W M Y N
Fresh, frozen, or canned strawberries	025	⌊⌊	D W M Y N
Fruit cocktail or jell-o salad with fruit	026	⌊⌊	D W M Y N
Raisin or grapes	027	⌊⌊	D W M Y N
Avocado	028	⌊⌊	D W M Y N

VEGETABLES

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Fresh tomatoes	029		D W M Y N
Canned tomatoes or tomato sauce	030		D W M Y N
Tomato juice, V-8 juice, vegetable juice	031		D W M Y N
Raw carrots	032		D W M Y N
Cooked carrots or carrot juice	033		D W M Y N
Corn	034		D W M Y N
Green or string beans	035		D W M Y N
Peas	036		D W M Y N
Baked, pinto, refried, kidney, or lima beans	037		D W M Y N
Mixed vegetables	038		D W M Y N
Broccoli	039		D W M Y N
Cauliflower	040		D W M Y N
Brussels sprouts	041		D W M Y N
Cabbage, cole slaw, or sauerkraut	042		D W M Y N
Red beets, not greens	043		D W M Y N
Sweet green, red, or yellow peppers	044		D W M Y N
Iceberg or head lettuce in salad	045		D W M Y N
Romaine or leaf lettuce in salad	046		D W M Y N
Raw spinach leaves in salad	047		D W M Y N
Cooked spinach	048		D W M Y N
Mustard, turnip, collard greens, chard	049		D W M Y N
Eggplant, zucchini, or summer squash	050		D W M Y N
Acorn, butternut, or other dark orange winter squash	051		D W M Y N
Onion as a cooked vegetable	052		D W M Y N
French fries, or other fried potatoes	053		D W M Y N
Baked, boiled, or mashed potatoes	054		D W M Y N
Yams or sweet potatoes	055		D W M Y N

OTHER DAIRY FOODS

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Cottage or ricotta cheese	056		D W M Y N
Cheddar, jack, swiss, mozzarella cheese	057		D W M Y N
Yogurt	058		D W M Y N
Cream cheese	059		D W M Y N

MEATS AND MAIN DISHES

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Hamburger	060		D W M Y N
Meatloaf	061		D W M Y N
Beef steak, roast beef, or beef brisket	062		D W M Y N
Casserole with beef and noodles	063		D W M Y N

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Roast beef or barbecue sandwich	064		D W M Y N
Beef or pork ribs	065		D W M Y N
Beef stew or potpie with vegetables	066		D W M Y N
Chili with meat and beans	067		D W M Y N
Beef, calf, or pig liver	068		D W M Y N
Lamb, roast, chops, or in stew	069		D W M Y N
Pork roast or pork chops	070		D W M Y N
Ham or ham sandwich	071		D W M Y N
Pork stew or pork pie	072		D W M Y N
Pork sausage in patties or links	073		D W M Y N
Bacon	074		D W M Y N
Eggs	075		D W M Y N
Venison, elk, or other game meat	076		D W M Y N
Pheasant, duck, or other game bird	077		D W M Y N
Fried chicken	078		D W M Y N
Baked or roasted chicken or turkey	079		D W M Y N
Chicken or turkey liver	080		D W M Y N
Chicken or turkey vegetable potpie	081		D W M Y N
Chicken or turkey sandwich	082		D W M Y N
Chicken salad or chef salad	083		D W M Y N
Tuna sandwich, salad, or casserole	084		D W M Y N

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Canned salmon, sardine, or oysters	085		D W M Y N
Fried fish or fish sticks	086		D W M Y N
Broiled or baked white-meat fish	087		D W M Y N
Fish sandwich	088		D W M Y N
Salmon, sardine, bluefish, swordfish	089		D W M Y N
Shrimp, lobster, or scallops	090		D W M Y N
Spaghetti or other pasta in tomato sauce	091		D W M Y N
Pizza	092		D W M Y N
Macaroni and cheese	093		D W M Y N
Enchilada	094		D W M Y N
Taco or tostada	095		D W M Y N
Burrito	096		D W M Y N
Hot dog	097		D W M Y N
Bologna, processed lunch meats, salami	098		D W M Y N
Polish sausages, brats	099		D W M Y N
Liverwurst	100		D W M Y N
Canned meats, spam or vienna sausages	101		D W M Y N
Soup (SPECIFY TYPE BELOW)	102		D W M Y N
What type of soup do you eat most often?			

CEREALS AND BREADS

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Cold breakfast cereal	103		D W M Y N
What types and brands of cold breakfast cereal do you eat most often?			
Oatmeal	104		D W M Y N
Other cooked breakfast cereal	105		D W M Y N
Instant breakfast beverage or bar	106		D W M Y N
Pancakes or waffles	107		D W M Y N
White bread	108		D W M Y N
Dark bread	109		D W M Y N
Dinner rolls, bagels, or pita bread	110		D W M Y N
White rice	111		D W M Y N
Corn bread or corn muffin	112		D W M Y N
Corn tortilla	113		D W M Y N
Flour tortilla	114		D W M Y N
Potato chips, corn	115		D W M Y N
Crackers: saltines, triscuit, wheat-thins	116		D W M Y N

OTHER FOODS

FOOD NAME	FOOD NO.	FREQ	PERIOD 1 2 3 4 5
Peanut Butter	117		D W M Y N
Peanuts	118		D W M Y N
Other nuts	119		D W M Y N
Butter	120		D W M Y N
Tub or liquid margarine	121		D W M Y N
Stick margarine	122		D W M Y N
Ice cream	123		D W M Y N
Ice milk, frozen yogurt, sorbet	124		D W M Y N
Chocolate candy	125		D W M Y N
Hard candy	126		D W M Y N
Cookies	127		D W M Y N
Pie	128		D W M Y N
Cake	129		D W M Y N
Doughnut, scones	130		D W M Y N
Jam, jellies, syrup	131		D W M Y N
Oat Bran	132		D W M Y N
Other Bran	133		D W M Y N
Wheat germ	134		D W M Y N
Olive oil	135		D W M Y N
Other oil dressing	136		D W M Y N
Mayonnaise	137		D W M Y N
Salad dressing	138		D W M Y N